
# *Think before you spit … and share:*

*Protecting consumers in Australia's direct-to-consumer health-related genetic testing (DTCGT) space*

*by*

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*'But it is not Pandora's Box that science opens; it is, rather, a treasure chest. We, humanity, can choose whether or not to take out the discoveries and use them, and for what purpose. Leaving the chest closed is not an option. Apart from anything else, if some of us don't open the chest visibly and benignly, others will do so secretly and perhaps malignly. Most of the treasures within can be used for either good or ill, but until we see them how can we tell?*

*John Sulston & Georgina Ferry, The Common Thread 2003*

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I declare that this thesis contains no material which has been accepted for a degree or diploma by the University or any other institution, except by way of background information and duly acknowledged in the thesis, and to the best of my knowledge and belief no material previously published or written by another person except where due acknowledgment is made in the text of the thesis.

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The research associated with this thesis was conducted under approval from the Tasmanian Social Sciences Human Research Ethics Committee, reference number H0013321.

Mary Jan Marcelline Charbonneau

July 2019

## Abstract

Traditionally health-related genetic testing was only available within the jurisdictional bounds of a country's healthcare system, subject to strict requirements for access, funding and actioning. Direct-to-consumer health-related genetic testing (DTCGT) represents a paradigm shift from medical to consumer, as private companies now provide health-related genetic tests and results directly to consumers in commercial transactions, typically conducted online.

Since 2007, when US company 23andMe invited the world to spit in a tube, pay a comparatively small fee, and discover its genetic roots and destiny, DTCGT has offered a future of hope, according to its proponents, and fear, according to its critics. DTCGT's key promise is *consumer empowerment* – that individuals armed with personal genetic information about their current and future health status will use it to make autonomous, informed decisions about their healthcare and lifestyles. Its critics, however, focus on the potential for *consumer harm*, especially psychological, in situations where individuals are required to self-interpret complex genetic information provided for bundles of different tests, and then determine for themselves how they feel and what they might do.

This research reports on modelling of Australia's DTCGT and clinical genetic testing (CGT) spaces and the results of an online panel survey. While the research focus is Australia, the online panel was conducted with 2000 respondents, 1000 each from Australia and the United States, with the United States results used to provide context and comparison. Modelling revealed what was initially believed to be a bifurcated system – consumer in the marketplace *or* patient in the clinic – had the potential for individuals to be both consumer *and* patient through consumer or company-initiated engagement with healthcare. Given current industry focus on monetisation of genetic data, DTCGT consumers can also assume the role of research participant by allowing use of their data in company research. As such, three distinct regulatory regimes are involved in the DTCGT space – medico-legal, consumer and human research – each affording different regulatory protections enlivened by DTCGT consumers' roles as consumer, patient *and* research participant.

In the survey component of this research, respondents were presented with sample DTCGT results for two disease predisposition tests and one pharmacogenomics test, randomly allocated into different risk and metabolisation rate treatments, and then asked to both interpret and contextualise results. The construct of 'match/mismatch' was developed based on consistency of personal interpretation with DTCGT disease predisposition results presented, and then applied to DTCGT engagement. Analysis demonstrated those who 'mismatched' experienced disproportionate *emotional distress* and *engagement*, and intended to engage in behaviours

unwarranted by actual results when compared to those who ‘matched’, providing evidence of potential consumer harm, especially psychological harm. The potential for harm to overall health was found relative to the pharmacogenomics test, with over one in ten respondents intending to independently alter their medication dosage based on results, and the potential for strain on healthcare resources as almost eight out ten intended to seek expert advice. Most notable overall was the similarity in response patterns between Australian and US respondents, suggesting at least a certain amount of 'universality' or response consistency in how individuals engage with DTCGT results.

The outcome of this research resulted in two key recommendations. First, given the pivotal role played by interpretation in engagement with DTCGT, the need for genetics education both for the general public and the medical profession was strongly recommended, not just to prepare both for DTCGT but for whatever the accelerating development of genetic tests, treatments and technologies brings. Secondly, with regard to regulatory reform, the recommendation was to do nothing UNTIL key players in the three regulatory spheres are brought together to consider DTCGT and future genetic offerings both in the clinic and the marketplace – from a holistic perspective. Australia’s DTCGT space demonstrates regulatory congestion – too many laws, areas of both overlap and gaps ripe for regulatory avoidance or commercial exploitation, with none totally fit for purpose. The traditional ‘siloed’ approach where each of these spheres regulates within its silo is no longer ‘fit for purpose’. The siloes need to be broken down and regulation developed from a holistic perspective as the window of opportunity to at least stay abreast of the commercialisation of genetics is rapidly closing.

## Acknowledgements

While a PhD is a solitary intellectual journey, it is not possible without support. First and foremost, I would like to thank the 4000+ respondents from Australia, the United States, the United Kingdom, and Japan who provided their considered opinions and responses in the online survey component of this research. While this thesis represents the views of respondents from Australia and the United States only, the data from all four countries has many more stories that I am eager to tell.

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## Publications and Presentations

The following publications and presentations arose from the work conducted for this thesis and the broader research project.

### *Peer-reviewed publications*

Jan Charbonneau, Dianne Nicol, Don Chalmers, Kazuto Kato, Natsuko Yamamoto, Jarrod Walshe and Christine Critchley, 'Public reactions to direct-to-consumer genetic health tests: A comparison across the US, UK, Japan and Australia' (2019) *Eur J Hum Genet* DOI:10.1038/s41431-019-0529-8.

Dianne Nicol, Tania Bubela, Don Chalmers, Jan Charbonneau, et al. 'Precision medicine: drowning in a regulatory soup?' (2016) 3(2) *Journal of Law and the Biosciences* 281-303.

### *Non-peer reviewed publications and commissioned research reports*

Jan Charbonneau, 答えは数字の中にある *General public engagement with direct-to-consumer genetic testing in Japan*, for the Graduate School of Medicine, Osaka University, Japan, November 2017.

Andelka Phillips and Jan Charbonneau, 'From the lab to the market: consumer understanding and direct-to-consumer genetic testing', *GeneWatch*, Oct – Dec 2015.

### *Presentations*

Jan Charbonneau, '*It's all in the numbers*: General public engagement with Direct-to-consumer genetic testing', Therapeutic Goods Administration, Canberra, Australia, November 2017.

Andelka Phillips and Jan Charbonneau, 'Giving away more than your genome sequence?: Privacy in the direct-to-consumer genetic testing space', *PrivacyCon*, Federal Trade Commission, Washington DC, United States, January 2016.

Jan Charbonneau, 'Think before you spit: ELSI and the direct-to-consumer genetic testing space', *Translation in Healthcare: Exploring the impact of emerging technologies*, University of Oxford, UK, June 2015.

Jan Charbonneau, 'Straight from the lab to the market: General public engagement with direct-to-consumer genetic testing', *DTC Genetics – Consumers, Contracts and Complexities*, King's College London, UK, June 2015.

Jan Charbonneau, 'Straight from the lab to the market: General public engagement with direct-to-consumer genetic testing', *European Society for Human Genetics*, Glasgow, Scotland, June 2015 (poster presentation).

Jan Charbonneau, 'Direct-to-consumer Genetic Testing: Regulating a moving target in a cloud', *Personalised Medicine Workshop*, University of Tasmania, Hobart, Australia, July 2014.

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# Chapter One:

# If you don't know where you're going...

any road will get you there.

Lewis Carroll *Alice's Adventures in Wonderland* 1865

# INTRODUCTION

In the mid 1800s, our understanding of the inheritance of genetic traits developed thanks to the efforts of Darwin and Mendel, explaining how each gene's interaction with the environment, and dominant or recessive nature, determined how it was passed on to subsequent generations. In the 1950s, the scientific discovery of the effect of an extra chromosome 21 and mutations in the CFTR gene quickly led to the development of diagnostic genetic tests for Down Syndrome and Cystic Fibrosis. By 1953 we understood both the structure and replication of deoxyribonucleic acid (DNA) − the source of all life − and by 1972 we could create as much synthetic DNA (rDNA) as we wanted. And by 2003, we had a sequenced reference genome courtesy of the collaborative efforts of those involved in the Human Genome Project − the Book of Life became readily available for all to read. While these developments occurred in research settings, laboratories and clinics, by 2007 23andMe was encouraging consumers to spit into tubes and discover their genetic destiny − all for a comparatively small fee.[1]

Relative to health-related genetic testing, this simple invitation to a 'spit party' has led to a paradigm shift from medical to consumer, as individuals can now access genetic tests previously only available in clinics. Private companies market genetic tests and provide results directly to consumers, typically in the online environment, effectively bypassing the healthcare system. Commercial involvement in genetics is not new, with direct to consumer health-related genetic testing (DTCGT) but the latest development in a long-standing tradition of commodification, monetisation and commercialisation of genes, genetic discoveries, and genetic technologies.

In 2011, Australia's National Health and Medical Research Council (NHMRC) stated: 'One of the most significant outcomes of the acceleration in genomic science is the development of personalised medicine … the capacity to predict disease development and influence decisions about lifestyle choices and to tailor medical practice to an individual.'[2] DTCGT has a role to play as it provides genetic information to a large number of individuals, fostering consumer empowerment relative to healthcare and lifestyle decision-making.[3] It has been suggested that

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[1] DTCGT company, 23andMe, features prominently as an example as a significant amount of its corporate information is in the public realm.

[2] National Health and Medical Research Council, Australian Government, *Clinical Utility of Personalised Medicine* (2011) <http://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/ps0001>. All URLs were operational at the time of writing, unless noted otherwise.

[3] See Don Chalmers, Dianne Nicol, Margaret Otlowski and Christine Critchley, 'Personalised Medicine in the Genome Era' (2013) 20(3) *Journal of Law and Medicine* 577-594; Sancy Leachman, Daniel MacArthur, Misha Angrist, Stacy Gray, Angela Bradbury and Daniel Vorhaus, 'Direct-to-Consumer Genetic Testing:

opening the technology to the general public may lead to 'more rapid advancement of knowledge' than could be achieved through academic or healthcare systems.[4] However concern has also been expressed about the ethical, legal and social implications of DTCGT and the potential for consumer harm, with these concerns judged by many as sufficiently serious to require regulation.

This research conducts an in-depth analysis of both the DTCGT and clinical genetic testing (hereafter referred to as CGT) for health-related purposes spaces. This represents the necessary first step, determining 'where we are' before assessing whether the current DTCGT regulatory space adequately protects consumers. To paraphrase Lewis Carroll, without a solid understanding of the space and how individuals engage with it, *ANY* regulation will suffice.

# PART ONE: FOCUSING THE RESEARCH

## *1.1.1 Focusing on the WHAT*

While a range of definitions exist for the term genetic test, this research adopts the US National Institutes of Health's definition of a 'medical test that identifies changes in chromosomes, genes or proteins', with such tests used to diagnose genetic conditions and determine individuals' chances of developing or passing on genetic disorders.[5] While genetic tests are available within the healthcare sector, the focus of this research is specifically on *health-related* genetic testing offered directly to consumers in commercial settings (DTCGT). While it is acknowledged DTCGT companies also offer other genetic tests such as ancestry, paternity, traits such as intelligence, and the clearly recreational such as consistency of ear wax, this research is only interested in the disease predisposition and pharmacogenomics tests on offer.[6]

While some DTCGT companies offer whole genome and exome sequencing, current price points put it out of the reach of the bulk primary target market for DTCGTs, and the complex data

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Personalized Medicine in Evolution' (2011) *Genomics Law Report* 34-40; Donato Ramani and Chiara Saviane, 'DCGT: the individual's benefits above all' (2011) 10(3) *Journal of Science Communication* C05.

[4] Sancy Leachman, Daniel MacArthur, Misha Angrist, Stacy Gray, Angela Bradbury and Daniel Vorhaus, 'Direct-to-Consumer Genetic Testing: Personalized Medicine in Evolution' (2011) *Genomics Law Report* 34-40, 39.

[5] Wherever possible, definitions are from the National Library of Medicine at the US National Institutes of Health <https://ghr.nlm.nih.gov/primer/testing/genetictesting>.

[6] The distinction between health-related and recreational is not clear-cut, with paternity and ancestry tests potentially having health implications as individuals discover their family histories.

generated would need professional interpretation to be of consumer utility.[7] As such, any reference in this research to DTCGT results refers to the more commonly employed analysis of single nucleotide polymorphisms (SNPs, commonly called snips).

Focusing on disease predisposition and pharmacogenomics brings DTCGT within the regulatory ambit of Australia's medical devices regulations, as both meet the initial bar of 'therapeutic'.[8] However, DTCGT, as a commercial offering, naturally falls within the regulatory ambit of Australia's consumer protection legislation and regulation. The *OECD Consumer Policy Tool Kit* adopted by Australian regulators suggests potential for financial and non-financial consumer detriment should be the primary focus when assessing whether policy reform or enforcement is warranted.[9] Regulators are encouraged to consider the scale of consumer detriment, which consumers are affected, and anticipated duration. Reform or enforcement action may be warranted if detriment is large but experienced by a small group of consumers (especially vulnerable consumers such as the elderly), or small but experienced by a large group of consumers.[10]

As consumer detriment drives both policy and enforcement, regulators need evidence-based data as to the potential for consumer detriment inherent in the DTCGT offering, which this research seeks to provide. Given concerns expressed in the literature about the potential for psychological harm in DTCGT, this research focuses specifically on personal non-financial hidden detriment – psychological detriment.[11]

### *1.1.2 Focusing on the HOW*

The traditional technique for legal research, commonly known as the doctrinal method, seeks to identify, interpret and apply 'relevant legal rules to practical human experience', and is broadly

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[7] Alex Keown, '23andMe kills its next generation gene sequencing project, cuts jobs' 27 October 2016 <http//www.pharmalive.com/23andme-kills-its-next-generation-gene-sequencing-project-cuts-jobs/>.
[8] *Therapeutic Goods Acts 1989* (Cth) s3 where 'therapeutic use' is defined as use in or in connection with (a) preventing, diagnosing, curing or alleviating a disease, ailment, defect or injury (*disease diagnosis*); s3(b) influencing, inhibiting or modifying a physiological process (*pharmacogenomics/nutrigenomics*); s3(c) testing the susceptibility of persons to a disease or ailment (*disease susceptibility*). See *Food, Drug and Cosmetics* Act 21 U.S.C. 321 s201(h).
[9] The Consumer Policy Toolkit does not prescribe but rather provides a non-exhaustive list of situation-specific examples for guidance.
[10] See Organisation for Economic Co-operation and Development, *Consumer Policy Toolkit* (OECD Publishing, 2010) DOI: 10.1787/9789264079663-en, 12.
[11] Detriment is something that causes damage, harm or loss.

characterised by an exhaustive literature review and close reading of case law and legislation.'[12] Or more simply stated, 'the formulation of legal 'doctrines' through the analysis of legal rules'.[13] While doctrinal research will always remain a significant part of legal research, it has increasingly been augmented by methods and theories from other disciplines, in particular, the social sciences. This represents a natural combination as both law and social sciences such as psychology and sociology which focus on human interaction, allowing law to adopt the hypothesis testing, experimentation and replication, often referred to as the 'scientific method', widely applied in both the social and physical sciences. 'Legal issues have always produced empirical questions' and the law has long looked beyond the traditional precedent or established law to answer them.[14] For example, in its landmark decision in *Brown v Board of Education of Topeka* 347 U.S. 483 (1954), the US Supreme Court relied heavily on social science research concerning harm caused to children from segregated education when finding racial segregation in schools unconstitutional.

The term 'evidence-based' is now used extensively in medicine, business and public policy parlance, as each routinely seek to subject core, widely accepted and actioned tenets to empirical testing. The concept itself as it relates to law is not new − as Florence Nightingale admonished the English Parliament in 1891 'you change your laws and your administration of them so fast and without inquiring after results past or present that it is all experiment...'.[15] Nor is applying empirical research methods new, with the Legal Realists considering 'law's social implications in the early 1900s'.[16]

Seeking out the best evidence available has now become common practice in law, with empirical research a 'regular feature in contemporary law reform'.[17] So much so, the Australian Law Reform Commission (ALRC) noted in 2011 that 'law reform recommendations cannot be based

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[12] Brendon Murphy and Jeffrey McGee, 'Phonetic legal inquiry an effective design for law and society research?' (2015) 24(2) *Griffith Law Review* 288-313, 288.
[13] Paul Chynoweth, 'Chapter Three Legal research', in Andrew Knight and Les Ruddock (eds.) *Advanced research methods in the built environment* (Wiley-Blackwell UK, 2008) 28-38, 28.
[14] Jeffrey Rachlinski, 'Evidence-based law' (2010-2011) 96 *Cornell L. Rev.* 901-923.
[15] Florence Nightingale's Letter to Sir Francis Galton, 7 February 1891 as quoted in Robert Boruch, 'Comparative aspects of randomised experiments for planning and evaluation', Chapter 17 in Martin Bulmer (ed) *Social Science Research and Government* (Cambridge University Press, 1987) 318.
[16] Felicity Bell, 'Empirical research in law' (2016) 25(2) *Griffith Law Review* 262-282, 262. Legal realism takes the view jurisprudence should rely on empirical evidence and testing hypotheses.
[17] Wendy Larcombe, Natalia Hanley, Bianca Fileborn, Nicola Henry and Anastasia Powell, 'Making good law: research and law reform' (2015) *University of Wollongong Research Online* <https://ro.uow.edu.au/cgi/viewcontent.cgi?referer=https://www.google.com/&httpsredir=1&article=3008&context=sspapers>.

upon assertion or assumption and need to be anchored in an appropriate evidence base.'[18] Applying a multidisciplinary lens to legal analysis and research ensures this is not done in isolation; recognising law is not confined to simply one aspect of human life but deals with all social, political, cultural and economic aspects.[19] A multidisciplinary approach is particularly on point for DTCGT, as different perspectives allow for '... anticipating products' ethical, legal and social implications *before* they are marketed and potentially injuring consumers psychologically or financially, and *before* they spark reactionary and short-sighted regulatory changes.'[20]

This research applies both law and consumer behaviour lens to DTCGT, utilising a mixed method approach. Consumer behaviour simply stated is ' the behaviour consumers undertake in seeking, purchasing, using, evaluating and disposing of products ... for personal consumption.'[21] Its inherent multidisciplinary approach recognises behaviours in the marketplace are subject to a range of internal, external and situational influences which vary by consumer and purchase decision, including emotions and sociocultural norms.

Doctrinal analysis of the existing regulatory space combined with empirical research modelling of both the CGT and DTCGT testing spaces provides insights from a system perspective. An online survey with embedded experimentation was used to analyse consumer engagement with sample DTCGT results, providing further insight from the perspective of those to be protected. Survey results also provide a lens through which to view other aspects of consumer engagement with DTCGT, and more broadly 'new genetics', 'personalised medicine' and whatever results from accelerating genetic discoveries and their clinical and marketplace translation − offering a glimpse of the future.[22]

This research does not present a theoretical exploration but rather maintains its focus on the current realities of the DTCGT market, its key players, and protections available. It is acknowledged key aspects of the academic discourse are not addressed in substantive detail, such as ethical considerations.

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[18] Australian Law Reform Commission, *Managing Discovery of Documents in Federal Courts*, Report 115 (2011), 1.41.
[19] See P Pandey, 'Problems and prospects of multidisciplinary approach in legal reasoning' (2011) 01(04) *Indian Journal of Humanities* 46-52.
[20] Jennifer Wagner, 'Interpreting the Implications of DNA Ancestry Tests' (2010) 53(2) *Perspectives in Biology and Medicine* 231-248, 246.
[21] Jan Charbonneau, Michael Solomon, Greg Marshall and Elnora Stuart, *Marketing: Real People, Real Choices* 2e (Pearson New Zealand, 2011) 132.
[22] The term 'translation' is used to denote the process whereby laboratory findings eventually lead to clinical tests, treatments, and marketplace offerings.

### 1.1.3 Focusing on the WHO

As the majority of DTCGT companies operate entirely or partially online and typically return results online, potential customers need to be Internet-literate, making this subset of the general public their primary target consumers. To both access and investigate the engagement of these potential DTCGT consumers with sample DTCGT results, an online panel survey was conducted contemporaneously in both Australia and the United States. While the focus is Australia, comparison with US responses provides context, establishing whether broad patterns exist, providing insight into how the Australian market might develop. Cross-country comparisons that identify significant similarities give weight to arguments for harmonisation of DTCGT guidelines, and the value of using experiences with regulation and research in one country to guide policy development in another. Cross-country comparisons identifying significant differences suggest the need for jurisdiction-specific regulation and research.

To date, no empirical research has been conducted comparing general public responses to DTCGT in Australia and the US.[23] While both are common law based with a similar DTCGT regulatory structure, they are at different stages of market development, providing interesting comparisons. The US has been at the forefront of DTCGT development with comparatively long-standing players such as 23andMe generating both extensive media coverage and regulatory attention. US consumers also have existing experience with commercial involvement in the medical sphere as direct-to-consumer advertising of prescription drugs has been in place since the 1980s.[24] Thus, the US is arguably a lead market, with Australia a lag market. A lead market is the first to successfully adopt an innovation, sending signals to lag markets about consumer acceptance of innovations, thereby reducing market and technological risk to their consumers and companies.[25]

Although a body of empirical research, mainly conducted in the US, exists, given its timing it represents mainly the experience of early adopters, which makes it difficult to extrapolate to the general public as a whole.[26] Early adopters are amongst the first to try new market offerings and generally have different motivations, attitudes and behaviours to those who purchase once

[23] Based on available public research to the best of the researcher's knowledge.
[24] See Natasha Parekh and William Shrank 'Dangers and opportunities of direct-to-consumer advertising' (2018) 33(5) *J Gen Intern* Med 586 – 7; Lee Ventola, 'Direct-to-consumer pharmaceutical advertising: Therapeutic or toxic?' (2011) 35(10) *P & T* 669 – 684.
[25] See Michael Spence, 'Job Market Signaling' (1973) 87(3) *Quarterly Journal of Economics* 355–374; Marian Beise, 'Lead markets: country-specific drivers of the global diffusion of innovations' (2004) 33 *Research Policy* 997-1018.
[26] See Cecile Janssens, 'The hidden harm behind the return of results from personal genome services: a need for rigorous and responsible evaluation' (2014) 20 November *Genetics in Medicine* DOI: 10.1038/gim.2014.169.

products are more firmly established.[27] Regulators need to gain an understanding of how non-early adopters might engage with DTCGT as they are the current focus of DTCGT marketing efforts, eager to capture their volume to increase profitability.

## PART TWO: STRUCTURE OF THE RESEARCH

This research is divided into seven chapters, including this Introduction. Chapter Two provides an overview of genetics and the key genetic discoveries and technological advances that have created the environment necessary for the efficient and effective operation of DTCGT companies. It discusses the challenges presented as DTCGT's disruptive nature created a paradigm shift from medical to consumer, and outlines DTCGT's key promise of consumer empowerment – that individuals armed with personal genetic information will use it to make autonomous informed healthcare and lifestyle decisions. For this promise to eventuate individuals must obviously purchase these products so purchase likelihood research and commercial market forecasts are explored.

Chapter Three presents the results of doctrinal analysis and modelling of both the CGT and DTCGT spaces. Each space is explored individually looking at the pathways to access, processes undertaken both by individuals and sector-wide, and the protections afforded, and then compared. What might appear initially as a bifurcated system, with individuals either patients *or* consumers, is shown to have the potential to intersect through either consumer or company-initiated engagement with healthcare, with consumers becoming patients. Investigating what individuals might do with genetic data is explored, identifying the potential sharing with family, online, and through participation in DTCGT research. The latter introduces a new role for DTCGT consumers – that of research participant. As such, individuals purchasing DTCGT products can be consumers, patients and research participants, afforded different protections from different regulations and oversight for each role. The regulatory response to date in the DTCGT sphere in both Australia and the US is also discussed.

The body of academic literature, government and organisational reports and empirical research is reviewed in Chapter Four. While DTCGT's promise is acknowledged, most of the discourse focuses on a range of concerns, which are presented in three key themes. The first, concerning the DTCGT offering, investigates questions about test validity, potentially onerous contract terms, whether

[27] See Jan Charbonneau, Michael Solomon, Greg Marshall and Elnora Stuart, *Marketing: Real People, Real Choices* 2e (Pearson New Zealand, 2011) Chapter 6; Everett Rogers, *Diffusion of innovations* 5e (Free Press, 2003).

consent obtained is informed, adequacy of privacy protections, and potentially misleading marketing messages. The second, concerning DTCGTs impact on the individual, focuses on how individuals interpret and contextualise complex genetic results, whether they experience psychological distress, and the behaviours prompted by test results, seeking to examine the extent to which engagement with DTCGT exposes consumers to potential harm. Perhaps the most significant concern expressed overall is the fact with DTCGT individuals are left to their own devices to interpret complex results from a range of tests and then decide, based on these interpretations, what to do. The third, concerning DTCGT's impact on healthcare systems, suggests DTCGT consumers will look to healthcare professionals for assistance and that the system is both under-resourced and unprepared to cope.

Chapter Five presents details of online survey development, including creation of embedded experiments, implementation, and analysis of results from the 2000 AU and US respondents. The core of the survey is the three sample sets of DTCGT results − two for disease predisposition and one for pharmacogenomics. Risk levels and metabolisation rate are manipulated with each respondent randomly allocated into one treatment for each set of results. Psychological outcomes and behavioural intentions are measured as well as other aspects of the DTCGT process, including purchase likelihood and willingness to participate in company research.

Results of the survey component are presented in Chapter Six. Given the small number of respondents with DTCGT purchase experience and comparatively low familiarity levels in both countries, the proportion of early adopters is small, with results representing the broader Internet-literate general public. Central is development and application of the 'match/mismatch' construct for the disease predisposition tests based on consistency of interpretation with risk treatment presented. This construct is then applied to both psychological outcomes experienced and behavioural intentions. While much of the existing empirical research focused on those who match − interpretation, affect and behaviour consistent with actual results − this research shifts the focus to those who mismatch. By using responses from those who match as benchmarks, analysis of those who mismatch can be explored to determine if they experience disproportionate psychological outcomes and intend to engage in behaviours not warranted by test results: in other words, are exposed to potential consumer detriment. Results from the pharmacogenomics experiment investigates whether the potential exists for physical harm to those who intend to independently alter medication regimes, and strain on healthcare resources from those intending to seek expert advice. High intention to engage with healthcare whenever offered would indicate coming strain on healthcare systems. A strength of this component is its testing of aspects of the

full DTCGT process, from familiarity to post-test determination of DTCGT confidence. Rather than focusing on nuanced detail, broad patterns of consistency are sought.

Chapter Seven is the final chapter and seeks to tie the threads together. Overall it seeks to determine whether more laws are needed in what is a state of 'regulatory congestion' with overlap and gaps ripe for regulatory avoidance and exploitation.

## CONCLUSION

For centuries humans have been interested in where we come from, how we become who we are now and will become in the future, and how we can use our knowledge to live healthier longer lives. If its promise eventuates, DTCGT may well contribute by empowering individuals to use genetic information to make informed decisions about their healthcare and lifestyles, perhaps not in terms of life quantity but certainly life quality. However, the simple act of spitting in a tube has resulted in significant challenges for all involved as

> '… scientists struggle to grasp the broad but nuanced legal implications of the technologies – a must if they wish to persuade society of their ability to self-regulate or of the potential disadvantages to premature or ill-conceived consumer protection legislation. … lawyers and policy makers struggle to understand the complex regulations or advocating consumer rights. … laypersons struggle to understand the scientific capabilities and limitations, as well as the legal implications of the retail DNA transaction, and hence struggle to understand the appropriate social meaning of or utility of the results that retail DNA companies provide them. …. clinicians struggle to understand the utility of these retail DNA tests and the legal or medical implications of incorporating the results when treating patients.'[28]

The following chapters delve into these challenges, especially those faced by consumers engaging with complex DTCGT results.[29]

[28] Jennifer Wagner, 'Interpreting the Implications of DNA Ancestry Tests' (2010) 53(2) *Perspectives in Biology and Medicine* 231, 231-232.

[29] Modelling of the DTCGT space and the survey component were conducted in 2015. Every effort has been made to reflect the regulations in place and state of the industry as at the time of writing.

# Chapter Two:

# It's all about YOU!

*'Today you are you. That is truer than true.*

*There is no one alive who is Youer than You.'*

Dr Seuss, *Happy Birthday to You* 1959

# INTRODUCTION

There are approximately 3 billion letters in the *Book of Life* – the human genome. That equates to over a quarter of a million pages of information divided into volumes for each of the genome's 23 chromosomes. On each page are row after row of A, C, G, and Ts in endless combinations – no other letters appear.[1] A mere 5 million of these make one human different from every other human – the rest are shared.[2] A T instead of an A or double C instead of CG, two X and three chromosome 21s and the individual is female with blue eyes … and Down syndrome.

In 2003 when the Human Genome Project (HGP) first published the *Book of Life*, researchers announced they had completed sequencing the entire human genome.[3] However, technological and scientific advances have resulted in new ways of interpreting the human genome, discovering daily what makes each human unique and importantly, why some inherit particular conditions or develop particular diseases.

This chapter provides the background context for the evidence-based component of the research and is divided into three parts. Part One provides an overview of the complex field of genetics: the study of heredity and variation in inherited characteristics. A short time ago this overview of genetics would have been considered novel and, by some, quite controversial – and a short time from now these basics may be radically out-of-date. Written by a non-geneticist/non-scientist, this is not meant to be comprehensive but rather an indication as to the information needed to interpret and action DTCGT test results. This part also discusses the role played by environmental factors and chance, necessary for contextualisation of results.

Part Two outlines key genetics discoveries and technology advances, from Mendel's peas and Watson and Crick's double helix, to the Human Genome Project and rapid sequencing technology. Each advance has led naturally to the emergence of DTCGT and illustrates commercial involvement in genetics is not new, nor is the tension between public and commercial spheres. In reality, DTCGT is but the latest development in a long-standing tradition of commodification, monetisation and commercialisation of genes, genetic discoveries, and genetic technologies.

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[1] These letters represent DNA's nitrogen bases: A stands for adenine, C cytosine, G guanine and T thymine.
[2] Riccardo Sabatini, 'How to read the genome and build a human being', (2016) *TED Talk* <https://www.ted.com/talks/riccardo_sabatini_how_to_read_the_genome_and_build_a_human_being>.
[3] Genetics Home Reference, 'What did the Human Genome Project Accomplish?' <https://ghr.nlm.nih.gov/primer/hgp/accomplishments>.

Part Three looks at the controversy surrounding DTCGT, its key promise of empowering consumers, turning them into active participants in their own healthcare decision-making rather than passive recipients of the medical sector's decisions, and the likelihood of the promise being realised. This brief section provides context for subsequent chapters. The processes and protections afforded individuals with both CGT and health-related DTCGT are addressed in Chapter Three, with the key areas of concern informing the survey development addressed in Chapter Four.

# PART ONE: GENETICS – HOW DID YOU BECOME YOU?

Part One outlines the current lay understanding relative to the fundamental building blocks of life, inheritance of genetic characteristics, genetic mutations at conception or developing through cell replication how genetic mutations, and the role genes play in disease development. This part finishes with discussion of the role played by both environment and chance − bad luck − in disease development.

*'Ex ovo omnia'- from an egg, everything'* [4]

## *2.1.1 Cells, proteins and genes*

All human life begins with a single cell – a zygote, the successful union of egg and sperm. The zygote divides into two daughter cells, beginning the process of embryonic development as cells continue to divide, making exact replicas of themselves with each division, until they have created the approximately 37 trillion cells in the average human body.

But how does this single cell – the zygote − result in a tiny human with all required organs, tissues and bones? While each cell is composed of the same nucleus and surrounding cytoplasm, the combination of proteins activated within it determines which of the over 200 types of cells it will become. Sperm and egg cells are referred to as germline, all others as somatic. Genes provide each cell with instructions needed to make these specific proteins. Simply stated, cells are the body's building blocks, proteins are the cells' building blocks, and genes are 'the blueprint'.

[4] William Harvey, *De Generatione Animalium* 1651.

### 2.1.2 Genes and chromosomes

Each cell in the human body has the same set of approximately 20,000 − 25,000 genes, tightly packed into 46 chromosomes in its nucleus. By comparison, fruit flies have 4 pairs, dogs 39 pairs and chimpanzees 24 pairs, making them humans' closest cousins.[5] A small chromosome (approximately 37 genes) exists in each cell's mitochondria, the components that break down nutrients to produce energy. Red blood cells contain nuclei when formed but this is replaced by haemoglobin when these cells mature to carry more oxygen.

Chromosomes differ in size depending on the number of genes contained and are present in pairs, one contributed by each parent. Twenty-two of the pairs are called autosomes and are the same in all humans, with the remaining pair, called sex chromosomes, determining gender. Females have two X chromosomes while males have an XY combination. All eggs carry X chromosomes. However there are two different types of sperm – carrying either the X or Y chromosome. Fertilisation by X sperm results in a female offspring while Y sperm results in a male offspring, meaning the male parent ultimately determines gender.

The genes within each chromosome are spaced out along long double-stranded molecules called deoxyribonucleic acid (DNA). DNA is made up of two strings of nucleotides coiled together into a double helix structure. A nucleotide consists of a sugar molecule attached to a phosphate group and a nitrogen base. DNA has four different nitrogen bases (A, C, G and T, referred to as the ACGT code). Each base pair (the connecting rungs on the double helix 'twisted ladder') is in the form of a covalent bond between two complementary nucleotides that follow precise pairing rules – A only bonds with T and C only bonds with G. When the double helix is separated, discovery of A on one of the strands means the corresponding base should be T, if not there is a variation. The genome contains approximately 3.1 billion of these base pairs.

Genes are sections of the ACGT code with defined start and stop positions providing instructions for protein manufacture, through a process called transcription and translation. Protein-coding genes account for about 1% of DNA. The DNA upstream of each gene contains special control sequences used by master controller molecules (promoters) to determine where to start and stop reading instructions. Genes are separated on DNA strands by long tracts of repetitive nucleotide sequences that do not encode protein. This 'junk DNA' was initially thought to have no function; hence the name coined by geneticist Susumu Ohno in 1972.[6] However subsequent research has

[5] <http://www.genome.gov/26524120>.
[6] Genetics Home Reference <https://ghr.nlm.nih.gov/primer/basics/noncodingdna>.

discovered these non-coding sequences provide, for example, sites where transcription is either activated or repressed.

### 2.1.3 Genes and proteins

Each gene's nucleotide sequences function as instructions for protein creation, dictating cell type and function. As genes are located in the cell's nucleus, instructions must be transmitted to ribosomes in the cytoplasm. Sequences are first transcribed onto a different molecule, known as ribonucleic acid (RNA), which passes through the cell's nucleus and transmits the ACGT codes to ribosomes. Like DNA, RNA is a chain of nucleotides but, unlike DNA, is single stranded and has the base uracil (U) instead of thymine (T). The RNA sequence is then divided up into components of three bases each, called codons, each of which carries the code for particular amino acids, which function as the building blocks for proteins. For example, GAG codes for glutamic acid, a key compound in cellular metabolism. Ribosomes in the cell cytoplasm use instructions in the codons to join together variable numbers and types of the twenty different amino acids to make the vast array of proteins needed for us to develop, grown and function. At the end of this process, the cell knows its type and function it should perform and can divide making an exact replica as required.

The epigenome is the chemical compounds and proteins that attach to DNA and direct various functions of genes – called marking. The 'marks' don't change the DNA sequence but rather the way the cells use the DNA instructions. As cells divide marks are passed to each new generation, allowing the new cells to retain their specialised functions. For a small number of genes, the epigenome determines whether the gene inherited from the mother or father is switched on. Abnormalities in this process, called imprinting, cause some diseases such as Prader-Willi syndrome characterised by insatiable appetite.

The epigenome can change during an individual's lifetime. Some of the chemical compounds in the epigenome come from natural sources while others are human-made (e.g. medicines). Lifestyle and environmental factors such as smoking, diet and infections can affect the epigenome and therefore chemical responses. Complex diseases such as cancer can be caused by changes in the genome, the epigenome or both. For example, a change in the epigenome might switch on or off genes involved in cell growth in a particular organ, resulting in the characteristic uncontrolled cell growth of most cancers.

When a cell divides, the DNA double helix 'unzips', breaking the loose covalent bonds between the base pairs. Nucleotides free floating in the nucleus hook up with nucleotides on each strand as per the pairing rules. For example, the AT pairing would split into A on one strand and T on the

other. The new T would then bond with the existing A on the one strand while the new A would bond with the existing T on the other strand. It takes approximately 8 hours for a single cell to reproduce.

Protein development and cell replication is not a one-time process but continues throughout foetal development and throughout the resulting human's lifespan. Throughout life, genes control the growth, daily maintenance, and overall functioning of the body. And the process is not just internal as cells constantly sense and interact with their external environment (e.g. nutrition). This process, called epigenetics, regulates and modifies gene expression but does not alter each gene's DNA sequence. Cells respond to external stimuli by sending internal signals to the genes, for example immune cells switching on antibody production in response to external toxins.

### 2.1.4 Genes and inheritance

*'The sole requirements for evolution are replication and inherited variation … the evolving organism must be able to reproduce itself, must do so imperfectly, and the variation must be transmitted to the next generation…. Once something is replicating with variation it will bit by bit explore the possibilities of its environment.'*[7]

Inheritance refers to the transmission of genetic characteristics from parent to child. Genes present in germline cells are the basic unit of inheritance and determine an individual's phenotype (observable traits), including the presence or predisposition towards conditions and diseases. Both genes and environment contribute to phenotype diversity, with some traits largely determined by one or the other.

#### 2.1.4.1 Autosomal dominant and autosomal recessive inheritance

The copies of each gene inherited from each parent (called alleles) on each autosomal chromosome (chromosomes 1 – 22) are either *dominant* or *recessive*. One autosomal dominant allele, from either parent, is required for phenotype presentation of a particular trait, meaning there is a 50% chance offspring will present and be a carrier. In some instances however, autosomal dominant disorders result from *de novo* mutations in early embryonic development, meaning while the parents are unaffected, the offspring may pass on the disorder to their children. As two autosomal recessive alleles are required for phenotype presentation, both parents must possess the gene, with resultant offspring having a 25% chance of inheritance; 50% chance of being unaffected but a carrier; and 25% chance of not being a carrier.

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[7] John Sulston & Georgina Ferry, *The Common Thread* (Corgi Books, 2003), 33.

### 2.1.4.2 Sex-linked inheritance

The Y chromosome contains a comparatively small number of genes whose functions are related to male sex determination, fertility, and characteristics such as male pattern baldness. As such, most sex-linked inheritance results from dominant and recessive alleles on the X chromosome. X-linked dominant characteristics such as Fragile X syndrome (developmental issues) more frequently affect females and the chance of inheritance differs between males and females, as males with X-linked characteristics cannot pass these to male offspring. X-linked recessive characteristics such as Haemophilia (blood clotting issues) more frequently affect males and there is no male-to-male X chromosome transmission. The second X chromosome in females may compensate for recessive mutations, whereas males will express all maternal-inherited X chromosome mutations.

### 2.1.4.3 Polygenic inheritance

With genetic characteristics involving only one gene, these inheritance patterns are straightforward. However, most genetic characteristics involve two or more genes at different loci (fixed position of genes on chromosome) on different chromosomes and may also involve environmental factors such as lifestyle. For example, at least 16 different genes are associated with eye colour, with the two most significant OCA2 and HERC2 on chromosome 15. Brown eye colour is dominant so only one allele of each gene is required while hazel, green, blue and grey are recessive, requiring two alleles.

Determining polygenic inheritance patterns can be quite complex. For example, while it is thought inheritance determines about 80% of an individual's height, factors such as nutrition also contribute. While more than 700 gene variants have so far been found, the precise effect of each on height has not been determined. Most produce small effects while others produce dramatic effects such as FGFRG gene variants causing achondroplasia (characterised by extremely short stature).[8] Height however is fairly straightforward compared to complex traits such as intelligence and complex diseases such as diabetes and cancer. This complexity is illustrated when considering the task involved in determining gene variants, identifying the overall effect of each variant and then using information in determining risk scores for polygenic diseases.

[8] Genetics Home Reference <https://ghr.nim.nih.gov/primer/traits/height>.

### 2.1.5 Genes and variation

All human beings have the same genes, with few exceptions such as the Y chromosome and individuals with chromosomal disorders. Within these genes however there are slight variations and it is these variations that make each human unique – making no one 'Youer than You'. These variations may be present from conception or may develop over an individual's lifetime as cells replenish and replicate.

#### 2.1.5.1 Mutations – spelling errors in the Book of Life

The process of cell division and replication is not infallible and is susceptible to variation or mutation, despite the body's robust control systems. Mutations can result from copying mistakes made during cell division, viral infections and chemical or radiation exposure. Once a mutation has occurred, each replicated cell will contain that mutation much like a spelling error appears in every photocopy made. While photocopies only contain original errors, mutations are an ongoing, cumulative process with original and new spelling errors replicated.

Mutations occurring in egg or sperm cells are referred to as germline mutations and can be passed on to offspring. Mutations occurring in somatic cells such as heart cells over an individual's lifetime are referred to as somatic mutations and are not passed on. Sometimes the mutation occurs in one small section of the ACGT code in a particular gene, sometimes an entire chromosome is missing, or an extra one is present. Monosomy occurs when one of the chromosomes from a pair is missing and results in diseases such as Turner syndrome where females born with only one X are infertile. Trisomy occurs when there are more than two of particular chromosomes, for example, Down syndrome resulting from an extra chromosome 21. The structure of the chromosome itself may be altered with portions missing (deletion), duplicated (duplication), transferred to another chromosome (translocation), or broken off and reattached upside down (inversion). Non-coding DNA is also subject to mutation, with the majority of random mutations occurring in these regions given there is far more non-coding than coding DNA.

Some mutations only create genotype diversity with no physical manifestation: genotype refers to the complete set of genes or, more narrowly, alleles responsible for particular traits. Others create observable phenotype changes, some of which are pathogenic, capable of causing disease with serious life limiting or life quality consequences. Mutations can manifest immediately such as Cystic Fibrosis (progressive respiratory and digestive disorder) or later in life such as Huntington's disease (progressive brain disorder).

#### 2.1.5.2 SNPs – the most common spelling errors

Single nucleotide polymorphisms or SNPs are the most common type of mutation. SNPs represents differences in single nucleotides, for example replacing a C with a T. SNPs occur on average once in every 300 nucleotides so there are approximately 10 million SNPs in the human genome. While most commonly found in DNA between genes, SNPs can also occur within particular genes or in regulatory sections of DNA.

While the vast majority of SNPs simply create basic genotype and phenotype diversity, they can also function as markers if there is known association with particular disease genes, allowing disease risk assessment and predicting drug responses.

### 2.1.6 Genes and disease

Genes have a role to play in all human disease development. Diseases result from inherited characteristics, germline and somatic mutations, and random genetic errors. Most chromosomal disorders result from random errors during reproduction rather than inheritance. Some diseases involve single (monogenic) or multiple genes (polygenic) while others result from interactions between multiple genes and environmental factors such as lifestyle (multi-factorial).

Genetic penetrance refers to the proportion of individuals with a particular genetic variant who express its associated trait. From a disease perspective, penetrance refers to the likelihood or probability individuals with a particular mutation will ultimately exhibit clinical symptoms of the associated disease or condition. Comparatively few diseases have complete penetrance, where all individuals with the particular mutations develop the associated diseases (2.1.6.1). Most diseases have incomplete penetrance with some individuals with the particular mutations developing the associated diseases and others not (2.1.6.2).

#### 2.1.6.1 Monogenic diseases

Monogenic disorders such as Cystic Fibrosis result from single gene mutations and are classified as dominant, recessive, or X-linked, following the straightforward patterns of inheritance discussed earlier. Dominant monogenic diseases result from inheriting one damaged allele while two damaged alleles are required for recessive diseases. X-linked monogenic diseases are linked to defective genes on the X chromosome and are also dominant or recessive. Genetic tests for such mutations are *definitive* with accurate diagnosis possible pre-conception for suspected carriers and at the pre-symptomatic stage for individuals, although time to present and severity of actual symptoms varies.

### 2.1.6.2 Polygenic and multi-factorial diseases

Monogenic diseases however represent only a small proportion of diseases, with most now believed to be polygenic or multifactorial. Polygenic diseases are associated with two or more genes and do not follow the straightforward patterns of inheritance, with the effects of genes believed to be cumulative, rather than simply dominant or recessive. When environmental factors are added in for multi-factorial diseases, the situation becomes even more complex resulting in diseases such as cancers.

Genetic tests for polygenic and multi-factorial diseases indicate individuals' *susceptibility* of developing specific diseases compared to the general population based on known genetic contributors. As these genetic variations can have small, large or cumulative effects, determining susceptibility becomes even more complex. For example, BRCA1/2 mutations greatly increase breast cancer risk while BARD1 and BRIP1 mutations increase risk to a smaller extent. Test results are *predictive* rather than definitive but may be used in healthcare decision-making e.g. increased susceptibility to colon cancer prompting more frequent screening.

### 2.1.6.3 The role of environment: Nature versus nurture

For centuries, scientists, academics and laypeople have debated whether nature (genes) or nurture (environment) is mainly responsible for determining who we are and who we become – from physical features to personality, to criminal tendencies and disease predisposition.[9]

Advances in computing power and data mining techniques coupled with expanding genetic and phenotype databases have led to a deeper understanding of the role played by environment. Illustrating the power of 'big data', researchers from Harvard and the University of Queensland mined an insurance database of nearly 45 million Americans, including more than 56,000 twin pairs and 724,000 sibling pairs, across 560 disease-related phenotypes to determine the relative contribution of genes versus shared environment. This 'big data' approach allowed analysis of hundreds of diseases rather than traditional one-disease-at-a-time studies. The first published study in 2019 investigating newborn to young adult twin pairs found overall 40% of diseases studied had a genetic component with 25% driven in part by shared environment. This approach allowed direct diseases comparisons finding, for example, cognitive disorders had the greatest

[9] See Francis Galton, *Men of Science Their Nature and Nurture* (D. Appleton and Company, 1875).

degree of heritability, with eye disorders and respiratory diseases having the highest environmental influences.[10]

However, it must also be remembered genetic susceptibility does not always imply genetic inevitability and the role of preventative measures cannot be discounted.[11] Even individuals in the same family with comparable genetic risk will not necessarily develop the disease or may vary in terms of onset, progression and symptom severity.

#### *2.1.6.4 The role of chance*

An oft-repeated quote suggests 'genetics loads the gun and environment pulls the trigger'.[12] Scientists now suggest that Lady Luck also contributes – perhaps identifying whose trigger gets pulled, or when. Research conducted in 2015 and 2017 suggested random errors during replication in normal stem cells were a major contributing factor to cancer development, with heredity and lifestyle playing a smaller role than previously believed.[13] This research, analysing 17 cancers in 423 cancer registries in 69 countries, suggested three random mutations with each cell replication, most of which are either not harmful or repaired by body's defences. While acknowledging contribution variation between different cancers, researchers concluded overall 66% of mutations resulted from replication errors, 29% environmental factors and 5% inheritance. The findings generated significant debate, with cancer researchers pointing out different cancers require different numbers of mutations to present, often in precise combinations with environmental factors, and that prevention still has a significant role to play.[14]

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[10] Chirag Lakhani, Braden Tierney, Arjun Manrai, Jian Yang, Peter Visscher and Chirage Patel, 'Repurposing large health insurance claims data to estimate genetic and environmental contributions in 560 phenotypes' (2019) *Nature Genetics* <https:doi.ord/10.1038/s41588-018-0313-7>.

[11] Australian Government, NHMRC, *Medical Genetic Testing Information for Health Professionals* (April 2010), 9 <https://www.nhmrc.gov.au/guidelines/publications/e99>.

[12] Extensive searches have not revealed the original source. For usage, see Soania Mathur, 'Genetics Loads The Gun and Environment Pulls the Trigger', 13 May 2013 *FoxFeedBlog*, Michael J. Fox Foundation for Parkinson's Research <https://www.michaeljfox.org/foundation/news-detail.php?soania-mathur-genetics-loads-the-gun-and-environment-pulls-the-trigger>.

[13] Cristian Tomasetti, Lu Li and Bert Vogelstein, 'Stem cell divisions, somatic mutations, cancer etiology and cancer prevention' (2017) 355 *Science* 1330-1334; Cristian Tomasetti and Bert Vogelstein, 'Variation in cancer risk among tissues can be explained by the number of stem cell divisions' (2015) 347(6217 *Science* 78-81.

[14] See National Health Service UK, 'Is bad luck the leading cause of cancer?', 27 March 2017 <https://www.nhs.uk/news/cancer/is-bad-luck-the-leading-cause-of-cancer/>; Sharon Begley, 'Most cancer cases arise from 'bad luck', 24 March 2017, *Scientific American* <https://www.scientificamerican.com/article/most-cancer-cases-arise-from-bad-luck/>; Rachel Thomson, 'Cancer all down to luck? No – we look behind the misleading headlines' *World Cancer Research Fund International*, Blog 7 January 2015. <https://www.wcrf.org/int/blog/articles/2015/01/cancer-all-down-luck-no-we-look-behind-misleading-headlines>.

For non-scientists or geneticists, perhaps the key contribution of this research has been to confirm how complex this field of study really is and how much more there is to discover.

If genes, environment and Lady Luck aren't complex enough, researchers are now investigating the role played by the microbiome – genes of microbes such as bacteria that live in and on the human body (microbiota). Researchers are investigating, for example, the microbiome's role in digestive health and its barrier effect in terms of the immune system.

# PART TWO: THE ROAD TO DTCGT – KEY MILESTONES IN THE EVOLUTION OF GENETICS AND GENETIC TESTING

Each of the following genetic discoveries and technologies have been fundamental to the evolution of our understanding of genetics and, when coupled with technological advances such as the Internet, e-commerce and computing power, have created a commercial environment ripe for the emergence of direct-to-consumer genetic testing.

## *2.2.1 Early discoveries: Fundamentals and terminology*

For centuries science has sought to understand the nature of inheritance – how traits are passed between generations. Darwin's 1859 'natural selection' suggested transmission of traits resulted from their successful interaction with organisms' environments, with those not increasing survival eliminated in subsequent generations. Darwin's research indicated from the outset that genetics did not act alone.[15] Mendel's 1866 pea experiments illustrated the underlying regularity of transmission of either dominant or recessive traits, establishing patterns of inheritance.[16] Early discoveries were also fundamental in developing the language of genetics such as *chromosomes* first observed in 1842,[17] *mitosis* in 1882,[18] and *deoxyribonucleic acid* (DNA) isolated in 1869.[19] The

[15] Charles Darwin, On the Origin of the Species by Means of Natural Selection, or, the Preservation of Favoured Races in the Struggle for Life (John Murray, 1859).
[16] Gregor Mendel, *Versuche über Pflanzen-Hybriden* (Brno, Verlag des Vereines 1866). See also Carl Correns, 'Mendel's Regelin über das Verhalten der Nachkomenscaft der Rassenbastarde' (1990) 18 *Bericht der Deutschen botanischen Gesellschaft* 158-168.
[17] Greek for colour (chroma) and body (soma), after dyes used to stain cells. Wilhelm Waldeyer 'Über Karyokinese und ihre Beziehungen zu den Befruchtungsvorgängen' (1888) 32 *Archiv für mikroskopische Anatomie und Entwicklungsmechanik* 1-122.
[18] Process whereby chromosomes double and evenly partition into two new cells from the Greek for 'thread'. Walter Fleming, *Zellsubstanx, Kern und Zelltheilung* (Leipzig, 1882) and <http://ghr.nlm.nih.gov/glossary=mitosis>.
[19] See Ralf Dahm, 'Friedrich Miescher and the discovery of DNA' (2005) 278 *Developmental Biology* 274-288.

term *genetics* was first used to describe the study of heredity in 1905,[20] with *gene* introduced in 1909 to describe Mendel's unit of inheritance, thereby distinguishing *genotype* from *phenotype*.[21]

One of the most significant modern advances occurred in 1953 when Watson and Crick identified the three-dimensional double helix structure of DNA and explained how it replicated.[22] The significance of this discovery was reflected in the awarding of the 1962 Nobel Prize in Physiology or Medicine to Watson, Crick and Wilkins. As Nobel Prizes are not awarded posthumously, Franklin's work on X-ray diffraction fundamental to the discovery of the double helix was not formally acknowledged.[23] Subsequent researchers focused on 'unravelling' the double helix, deciphering individual genes, determining specific mutations resulting in hereditable diseases and developing genetic tests for clinical application. For example, 1956 saw discovery of haemoglobin alterations causing Sickle Cell Disease (red blood cell disorder)[24] and definitive confirmation human cells contain 46 chromosomes presenting in pairs,[25] and 1959 the extra chromosome 21 responsible for Down Syndrome.[26] The 1968 Nobel Prize in Physiology or Medicine was awarded to US National Institutes of Health (NIH) scientists Nirenberg, Khorana and Holley for 1966 research determining how information in DNA translated into amino acids, the building blocks of protein.[27]

Genetic advances have been coupled with, and facilitated by, technological advances. In 1972 scientists developed methods for isolating, amplifying and precision moving of DNA segments or genes. This process for creating genetically modified DNA (recombinant DNA or rDNA) involved chemically cutting and splicing then inserting hybrid genetic material in host cells, usually bacteria.[28] To create rDNA, base pairs were moved in new locations in originating DNA or added from other DNA sources, transferring source characteristics to hosts. This 'molecular cloning'

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[20] William Bateson <http://www.dnalc.org/view/16195-Gallery-5-William-Bateson-Letter-page-1.html>.
[21] Wilhelm Johannsen, *Elemente der exakten Erblichkeitslehre* (Verlag Von Gustave Fischer, 1909).
[22] James Watson & Francis Crick, 'Molecular Structure of Nucleic Acids' (1953) 171(4356) *Nature* 737-738.
[23] See <http://www.nobelprize.org/nobel_prizes/medicine/laureates/1962/>.
[24] Vernon Ingram, 'Specific chemical difference between the globins of normal human and sickle-cell anemia haemoglobin' (1956) 178 *Nature* 792-794.
[25] Joe Hin Tjijo and Albert Levan, 'The chromosome number in man' (1956) 42 *Heredita* <https://doi.org/10.1111/j.1601-5223.1956.tb03010.x>.
[26] Jermome Lejeune, Marthe Gautier and Raymond Turpin, 'Etude des chromosomes somatique de neuf enfants mongoliens' (1959) 248 *Comptes rendus de l'Académie des Sciences* 1721-1722.
[27] See <http://www.nobelprize.org/nobel_prizes/medicine/laureates/1968/>.
[28] Stanley Cohen, Annie Chang, Herbert Boyer and Robert Helling, 'Construction of Biologically Functional Bacterial Plasmids in vitro' (1973) 70(11) *Proceedings of the National Academy of Sciences* 3240-3244; David Jackson, Robert Symons and Paul Berg, 'Biochemical method for inserting new genetic information into DNA of Simian Virus 40: circular SV40 DNA molecules containing lambda phage genes and the galactose operon of Escherichia coli' (1972) 60(10) *Proceedings of the National Academy of Sciences* 2904-2909.

allowed scientists to produce whatever specific DNA in whatever quantity was needed for their research, accelerating the rate of genetic discovery. Berg, Gilbert and Sanger shared the 1980 Nobel Prize in Chemistry for this fundamental discovery.[29] The 1970s saw development of rapid DNA sequencing methods and standardised sequencing protocols, providing more cost and time effective methods greatly accelerating biological discovery, medical research and translation into clinical applications. For example, the Sanger's 1975 method for attaching markers to growing ends of DNA chains is still used in most research and commercial laboratories.[30]

Not only did rDNA methods revolutionise molecular biology, but they also triggered commercial applications, kick-starting the 'business of genetics'.

### 2.2.2 *Commercialisation: The business of genetics and genetic discoveries*

Those seeking to monetise discoveries and technology have often sought patent protection: legally enforceable exclusive rights to commercially exploit new, innovative and useful devices, substances, methods or processes for specific terms in exchange for full disclosure.[31] Patents have been particularly important in the development of the research-intense biotechnology sector that develops technology and products based on biological processes.[32] Biotech companies however generally do not commercialise their own inventions but rather directly sell or license rights to sell to other entities such as pharmaceutical companies, requiring the legal protection afforded them by patents.[33]

One of the first biotechnology patent was formally granted in 1980 for specific rDNA methods developed by Cohen and Boyer, generating lucrative licensing revenues of US$255 million during

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[29] See <http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1980/berg-facts.html>.
[30] Frederick Sanger and Alan Coulson, 'A rapid method for determining sequences in DNA by primed synthesis with DNA polymerase' (1975) 94 *Molecular Biology* 441-448; Stanley Cohen, Annie Chang, Herbert Boyer and Robert Helling, 'Construction of biologically functional bacterial plasmids in vitro' (1973) 70(11) *Proceedings of the National Academy of Sciences* 3240-3244; Angelo DePalma, 'Sanger sequencing: Still the gold standard? (2018) November 5 *Lab Manager*; Armando Totomoch-Serra, Manlio Marquez and David Cervantes-Barragan, 'Sanger sequencing as a first-line approach for molecular diagnosis of Andersen-Tawil syndrome' (2017) 1(6) *F1000Res.* DOI: 10.12688/f1000research.11610.1.
[31] For AU requirements see the *Patents Act 1990* (Cth) s7 regarding novelty, inventive step and innovative step, s7A usefulness and s13 exclusive rights granted. For US requirements see the U. S. Patent Act 35 USC. Chapter 10: Patentability of Inventions and § 102 novelty and § 103 non-obvious subject matter.
[32] Organisation for Economic Co-operation and Development, *An Overview of Biotechnology Statistics in Selected Countries* (2003).
[33] Organisation for Economic Co-operation and Development, *An Overview of Biotechnology Statistics in Selected Countries* (2003); Esteban Burrone, 'Patents at the Core: the Biotech Business', World Intellectual Property Organisation <http://www.wipo.int/sme/en/documents/patents_biotech.htm>.

its lifetime to their respective academic institutions, consistent with academic commercialisation models.[34] Boyer however sought to personally capitalise, in 1976 co-founding Genentech, a clearly profit-seeking entity. Amongst Genentech's many accomplishments included isolation of genes leading to the development of synthetic human insulin, the first rDNA drug.[35] Licensee Eli Lilly & Co began marketing this synthetic insulin in 1982.[36]

To illustrate the increasing commercialisation of discoveries, consider that in 1921 Banting and Best, the discoverers of insulin, sold their patent rights to the University of Toronto for CDN$1 each.[37] In 1923, the university gave royalty-free manufacturing rights to Eli Lilly amongst others to create insulin from animal pancreases. While the university's intention was to keep prices down for the then life-saving drug, subsequent commercialisation of synthetic insulin has resulted in ever increasing prices, burdening both individuals and healthcare systems.

In 1982, a human gene patent was formally granted for synthesized DNA (cDNA).[38] To illustrate patents' lucrative nature, commercialisation of its erythropoietin gene patent into anaemia treatment has generated Amgen US$1.5 billion annually.[39] Most importantly, these and other patents firmly established DNA as a commodity capable of significant monetisation, setting the stage for the eventual commercialisation of genetic testing.

While lucrative, gene patents have also been extremely controversial, best illustrated by the case of Myriad Genetics' BRCA 1 and 2 patents, commercialised into the BRACAnalysis® diagnostic, generating US$400 million in 2011 alone.[40] Myriad's aggressive patent enforcement arguably led to higher prices, restricted access, and eventually protracted litigation in multiple countries.[41] In 2013, after five years of litigation, the US Supreme Court in *Association of Molecular Pathology Et*

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[34] Center for Public Genomics Seminal Genomic Technologies – Cohen-Boyer and Recombinant DNA, <http://www.genome.duke.edi/centers/cpg/case-histories/seminal-genomic-technologies/cohen-boyer/>.
[35] See US FDA 'Celebrating a Milestone: FDA's Approval of First Genetically-Engineered Product' <http://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/SelectionsFromFDLIUpdateSeriesonFDAHistory/ucm081964.htm>.
[36] See Gary Pisano, 'Can Science Be a Business? Lessons from Biotech' (2006) 84(10) *Harvard Business Review* 114-124.
[37] See, for example, <http://www.cdnmedhall.org/inductees/frederickbanting> and <https://heritage.utoronto.ca/exhibits/insulin>.
[38] See US Patent 4,363,877 for cDNA encoding human growth hormones.
[39] Lori Andrews, 'The Gene Patent Dilemma: Balancing Commercial Incentives with Health Needs' (2002) 2 *Journal of Health Law & Policy* 65-106.
[40] See Lane Baldwin and Robert Cook-Deegan, 'Constructing narratives of heroism and villainy: case study of Myriad's BRACAnalysis® compared to Genentech's Herceptin®' (2013) 5(8) *Genome Medicine* <http://genomemedicine.com?content/5/1/8>.
[41] See Bryn Williams-Jones, 'History of a Gene Patent: Tracing the Development and Application of Commercial BRCA Testing' (2002) 10 *Health Law Journal* 123-146.

*Al. v. Myriad Genetics, Inc., Et Al.* 569 US 576 (2013) definitively established human genes in natural form were not patentable but allowed patenting in synthetic form (cDNA). In 2015, Australia's High Court in *D'Arcy v Myriad Genetics Inc.* [2015] HCA 35 declared genes in both natural *and* synthetic form do not constitute a patentable invention, with the majority ruling the key patent claim was to information contained in genes rather than their physical structure.

### *2.2.3 The Human Genome Project: Writing the Book of Life*

With automation of DNA sequencing, researchers shifted their focus to the entire human genome, seeking to determine base pair order in DNA segments (sequencing) and the position of genes on chromosomes (mapping).[42] The Human Genome Project (HGP) began in 1988 with an estimated timeline of 15 years, an eventual budget of US$3billion and the 'audacious goal of providing the tools to uncover the hereditary factors in virtually every disease'.[43]

Deciphering the human genome however also attracted corporate attention. In 1998 former NIH scientist Craig Venter started Celera Genomics with funding of a comparatively modest $US300 million. Celera's mission was to complete sequencing within three years, patent resultant data and sell it via subscription.[44] Venter's action sparked a scientific race 'billed by some as a moral and ethical contest pitting publicly funded science ... against commercialised research'.[45] The HGP highlighted, on the world stage, the tension between public science and commercial interests but also the speed with which discoveries could be made in the commercial sector and the sector's clear intention to monetise these lucrative discoveries.

Celera ultimately did not obtain patent protection for its annotated database, as it did not meet the US Patent Office utility guidelines requiring specific, substantial and credible utility.[46] Its commercialisation plans were also hindered by the HGP's commitment to rapid data release and public access to primary genomic sequences. Referred to as the 1997 Bermuda Principles, the expectation was that DNA sequenced information would be released without restrictions into

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[42] See <http://www.genome.gov/11006943> for sequencing and Genetics Home Reference <http://ghr.nlm.nih.gov/glossary=mappedgene> for mapping.
[43] See 'An overview of the Human Genome Project' <http://www.genome.gov/pfv.cfm?pageID=12011239>. See Francis Collins, 'Shattuck Lecture – Medical and Societal Consequences of the Human Genome Project' (1999) 341(1) *New England Journal of Medicine* 28-37; 'Understanding Our Genetic Inheritance: The Human Genome Project, The First Five Years, FY 1991-1995' <http://web.ornl.gov/sci/techresources/Human_Genome/project/5yrplan/firstfiveyears.pdf>.
[44] Celera Genomics corporate history <https://www.celera.com/celera/history>.
[45] 2018 obituary of Sir John Sulston <https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)30735-9/fulltext>.
[46] See US Department of Commerce, Patent and Trademark Office *Utility examination guidelines* 3 January 1995, <https://www.uspto/gov/web/offices/com/sol/notices/101guide/pdf>.

publicly available databases within 24 hours of generation.[47] In addition to the actual data, this open access was one of the HGP's significant outcomes. It must be noted, however, that the same open access also benefited the commercial sector, providing them with much needed, scientifically validated data – at no cost.

A draft sequence covering 90% of the human genome was announced in mid-2000, with then President Bill Clinton stating understanding the human genome 'holds an extraordinary trove of information about human development, physiology, medicine and evolution' leading to 'new ways to prevent, diagnose, treat, and cure disease'.[48] In a joint announcement with then UK Prime Minister Tony Blair, Clinton further suggested '... it is now conceivable that our children's children will know the term ''cancer'' only as a constellation of stars.'[49]

In 2001, the HGP published its draft sequence in respected publication *Nature*.[50] Concurrently, Celera's draft sequence was published in sister publication *Science*.[51] In 2003, the HGP's scientists from the US, UK, Japan, France, Germany and China completed sequencing the human genome 'within the limits of today's technology ', approximately 99%, coming in under budget at $US2.7billion.[52]

### *2.2.4 Deciphering the human genome: Reading the Book of Life*

While the precise genetic blueprint of each individual is unique, HGP data functioned as a 'reference genome', thereby rapidly accelerating the speed at which genetic mutations could be identified. For example, isolating the Cystic Fibrosis gene in 1989 was the result of 9 years of painstaking searching. By comparison, use of HGP data resulted in the genetic mutation responsible for Parkinson disease being mapped in 9 days.[53]

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[47] See <http://www.genome.gov/25520385>.
[48] The White House, Office of the Press Secretary, 26 June 2000 <https://www.genome.gov/10001356/june-2000-white-house-event/>.
[49] Government Publishing Office, President William Clinton, Remarks on Completion of the First Survey of the Human Genome Project June 26, 2000<https://www.govinfo.gov/content/pkg/WCPD-2000-07-03/pdf/WCPD-2000-07-03-Pg1499.pdf>
[50] International Human Genome Sequencing Consortium, 'Initial sequencing and analysis of the human genome' (2001) 409 *Nature* 860, 860-921.
[51] Craig Venter, Mark Adams, Eugene Myers, Peter Li, Richard Mural et al. 'The sequence of the human genome' (2001) 291(5507) *Science* 1304-1351.
[52] See <http://www.genome.gov/11006943>.
[53] Human Genome Project Information, 'President Clinton announces the completion of the first survey of the entire human genome' (Press Release) 25 June 2000. <http://web.ornl.gov/sci/techresources/Human_Genome/project/clinton1.shtml>.

While the initial sequence carried a price tag just under US$3 billion and took 13 years, technological improvements have resulted in increasingly faster and more cost-efficient whole genome (WGS) and exome sequencing (WES). With WGS, nucleotides along the entire genome (approximately 95%) are analysed while exome sequencing analyses DNA coding functional proteins (approximately 2%). By 2007 the cost to sequence DNA pioneer James Watson's genome was less than US$1.5 million and took just four months.[54] In 2013, DNADTC began offering whole genome sequencing directly to consumers for approximately US$7000 with turnaround between 10 and 14 weeks.[55] In late 2018, Veritas Genetics lowered its $999 whole genome sequencing and interpretation service to $199 for two days as both a promotion and a signal that a $99 price point was in sight.[56] While physicians must order tests, results are returned directly to consumers. It was suggested in 2010 a price point of $1000 was needed for sequencing to become affordable to the wider public - a point it appears we have reached.[57]

From the outset, those involved in the HGP realised the project would have 'profound long-term consequences for medicine' but the 'accelerated pace of genetic discovery' would also raise significant ethical, social and legal implications (ELSI) with funded research beginning in 1990.[58] The National Human Genome Research Institute in their 2011 strategic plan identified psychosocial and ethical issues in genomic research and medicine such as protection and expanded diversity of research participants and interpretation of DTCGT results, as well as legal and policy issues, including intellectual property protection and regulating commercialisation.[59]

### *2.2.5 From genome sequencing to large-scale genetic testing: Setting the stage for DTCGT*

While many viewed mapping the human genome as a finite end in itself, those most intimately involved noted '… it has not escaped our notice that the more we learn about the human genome, the more there is to explore.'[60] The article announcing to the world the blueprint of life

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[54] Meredith Wadmna, 'James Watson's genome sequenced at high speed' (2008) 452 *Nature* 788.
[55] See <http://www.dnaDTCGT.com>.
[56] See <www.veritasgenetics.com>; Megan Molteni, 'Now you can sequence your whole genome for just $200' *Wired* 19 November 2018 <https//www.wired.com/story/whole-genome-sequencing-cost-200-dollars/>.
[57] Kevin Davis, The $1000 Genome: The Revolution in DNA Sequencing and the New Era of Personalized Medicine (Free Press, New York, 2010).
[58] International Human Genome Sequencing Consortium, 'Initial sequencing and analysis of the human genome' (2001) 409 *Nature* 860-921, 914. See also <http://www.genome.gov/10001618>.
[59] Eric Green, Mark Guyer & National Human Genome Research Institute, 'Charting a course for genomic medicine from base pairs to bedside' (2011) 470 *Nature* 204-213, 210.
[60] International Human Genome Sequencing Consortium, 'Initial sequencing and analysis of the human genome' (2001) 409 *Nature* 860-921, 914.

ended with a quote from poet T.S. Eliot, a quote embedded with a promise: 'We shall not cease from exploration. And the end of all our exploring will be to arrive where we started, and know the place for the first time.'[61]

Prior to the HGP's completion, Francis Collins generated excitement and expectations when he foretold the role of genetic testing in the coming age of personalised medicine in the 1999 Shattuck lecture. Collins described a future where in 2010, John, a young adult, would provide his doctor with a DNA cheek-swab and informed consent for a battery of genetic tests, opting only to be tested for disorders with clinically validated preventive measures. These tests would indicate reduced risk for prostate cancer but increased risk for colon cancer, lung cancer and coronary disease, prompting annual colonoscopies and successful efforts to quit smoking. A prophylactic drug regime based on John's genetic data would be prescribed to reduce cholesterol and coronary risk.[62]

Seeking to create Collins' 'brave new world', the focus changed to developing genetic tests, translating laboratory findings into tests allowing more precise diagnosis. The reference genome accelerated the pace at which the individual genes and gene combinations contributing to disease could be isolated and diagnostic tests developed. Technological advancements eventually allowed for high-throughput processing, reducing time needed and multiplex testing of one sample for multiple markers and diseases.

With genetic testing, DNA is extracted from blood, tissue or bodily fluid samples and then analysed for the specific biochemical, chromosomal or genetic markers. Markers used are known to be linked to genetic mutations that definitively diagnose genetic disorders or indicate increased disease susceptibility an individual or their progeny (carrier status), as well as potential responses to drug therapies (pharmacogenomics) or nutritional regimes (nutrigenomics).

Developing genetic tests for diagnosis post-discovery is not new. In 1983, the first disease gene was mapped to a specific chromosome when the team led by James Gusella isolated the chromosome mutation resulting in Huntington disease.[63] Discovery quickly led to the

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[61] Ibid. Quoting from T. S. Eliot, *T. S. Eliot. Collected Poems 1909-1962* (Harcourt Brace, New York, 1963).
[62] Francis Collins, 'Shattuck Lecture – Medical and Societal Consequences of the Human Genome Project' (1999) 341(1) *New England Journal of Medicine* 28-37.
[63] James Gusella, Nancy Wexler, Michael Conneally, Susan Naylor, Mary Anne Anderson, Rudolph Tanzi, Paul Watkins, Kathleen Ottina, Margaret Wallace, Alan Sakaguchi, Anne Young, Ira Shoulson, Ernesto Bonilla & Joseph Martin, 'A polymorphic DNA marker genetically linked to Huntington's disease' (1983) 306 *Nature*, 234 – 238.

development of the diagnostic test, establishing the pattern of discovery followed by clinical application.

Since 2005, genome-wide association studies (GWAS) have accelerated the rate at which multiple markers on multiple genes contributing to complex diseases have been identified, compared to previously used single gene approaches.[64] GWAS use high-throughput genotyping technologies to assay SNPs in a case-control approach where genomes of those with particular conditions are compared with control groups, with data used to calculate odds ratios. The odds of disease in affected participants are compared with control groups with odds ratios of >1 indicating some and >1.5 modest association to disease studied.[65] The more SNPs linked to particular diseases, the more refined the resulting predictive diagnostic tests. While more rigorous methodologies have been developed and sample sizes increased, GWAS have generally been conducted with specific populations such as those with European ancestry, leading to questions as to whether known disease markers are applicable to different populations.[66] GWAS can also generate false positive and false negative results. As such, the predictive value of SNPs and broad-based applicability is constrained by the quality of GWAS.

More precise genetic analysis also allows for more reliable prediction of disease progression and effective treatments. The emerging field of precision medicine focuses on identifying *which* treatment approaches will be the most effective for *which* patients based on genetic, environmental and lifestyle factors.[67] This contrasts with previous approaches where treatment and prevention strategies were developed for the average person and administered in a 'one size fits all' approach. Pharmacogenomics combines pharmacology and genomics to develop medications and determine dosages tailored to genetic variations. In one success story, more precise genomic categorisation of breast cancer has resulted in targeted prescribing of Herceptin®. Not only is the drug costly, generating Genetech US$5.728 billion in 2011 alone, but has

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[64] See Robert Klein, Caroline Zeiss and Josephine Hoh, 'Complement Factor H Polymorphism in Age-Related Macular Degeneration' (2005) 308(5720) *Science* 385-389.
[65] Thomas Pearson and Teri Manolio, 'How to Interpret a Genome-wide Association Study' (2008) 299(11) *Journal of the American Medical Association* 1335-1344.
[66] Pauline Ng, Sarah Murray, Samuel Levy and Craig Venter, 'An agenda for personalized medicine' (2009) 461(8) *Nature* 724-726.
[67] National Research Council 'Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease' (2011). <https://www.plengegen.com/wp-content/uploads/4_Toward-Precision-Medicine.pdf>.

significant side effects that outweigh any potential benefits for some.[68] Tailoring of medication and dosages to an individual's genetic makeup minimises side effects and results in improved prognoses.[69] Screening allows at-risk patients to be alerted early, allowing for preventative medical intervention or lifestyle changes.[70]

Each of these genetic discoveries and advances were fundamental in creating the technological and economic environment necessary for commercial genetic testing to represent a viable business proposition.

# PART THREE: DTCGT - OUT OF THE CLINIC AND ONTO THE WEB

## *2.3.1 DTCGT: The logical next step ... but controversial from the outset*

*'Despite being on the market for nearly a decade, direct-to-consumer (DTC) genetic testing continues to be controversial among experts and raises concerns among health care providers and regulatory agencies.'*[71]

Traditionally, CGT has only been available within each country's healthcare system. Since the late 1990s, the corporate sector has been offering genetic testing for paternity (biological relationship) and ancestry (geographic origin) directly to consumers. In the mid 2000s the corporate sector began also offering health-related genetic testing (DTCGT) directly to consumers. Early pioneers in the DTCGT sector included 23andMe (2006, US) Navigenics (2007, US), deCODEme (2007, Iceland) and Pathway Genomics (2008, US) with tests offered ranging from the medically significant such as diabetes to the innocuous such as earwax consistency.[72]

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[68] Lane Baldwin and Robert Cook-Deegan, 'Constructing narratives of heroism and villainy: case study of Myriad's BRACAnalysis® compared to Genentech's Herceptin®' (2013) 5(8) *Genome Medicine* <http://genomemedicine.com?content/5/1/8>.
[69] Australian Government, NHMRC, *Clinical Utility of Personalised Medicine* (2011), 6.
[70] 'President Clinton announces the completion of the first survey of the entire human genome' (Press Release) 26 June 2000 <https://www.genome.gov/10001356/june-2000-white-house-event/>.
[71] Brigham and Women's Hospital, 'Studies probe value and impact of direct-to-consumer genetic testing' *ScienceDaily* 13 December 2016. <https://www.sciencedaily.com/releases/2016/12/161213174952.htm>.
[72] See Andelka Phillips, 'Data on direct-to-Consumer Genetic Testing and DNA testing companies', 19th February 2018, DOI: 10.5281/zenodo.117922 for a comprehensive list.

DTCGT has been called 'one of the most promising, yet controversial medical advances of the modern era'.[73] With DTCGT, individuals order tests, provide DNA and receive results (typically online) directly from companies bypassing traditional healthcare gatekeepers, representing a paradigm shift from medical to consumer spheres.

DTCGT is a 'natural entrepreneurial offshoot' of the HGP with its release of freely available sequencing data and open-access, peer-reviewed publication of genetic findings as expected in academic and research institutions.[74] The DTCGT industry has capitalised on the increasing number of published GWAS identifying genetic variants needed for test development, technological developments such as high throughput analysis decreasing costs per unit analysed, and protection provided by patents for any independent discoveries made.[75] DTCGT's business model of 'cutting out the middleman' is consistent with current online business models, and capitalises on consumers' increased uptake of e-commerce, and use of the Internet for health-related purposes.[76]

From the outset, commercial DNA testing has been controversial with the DNA ancestry testing sector criticised for 'selling the imprimatur of science', invoking ''science's power without accepting its limits' and failing to make clear 'the limitations and potential dangers'.[77] Wagner noted that 'The retail DNA industry is forcing laypersons, academics, and medical and legal professionals alike to face the crossroads of genetics, law and society.'[78] And, since 23andMe invited Americans to its first 'spit party' in 2007, the controversy has only intensified.[79]

DTCGT was always going to be particularly controversial as it represents a disruptive innovation, offering new services that do not fit neatly into existing medical or consumer regulatory

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[73] Sancy Leachman, Daniel MacArthur, Misha Angrist, Stacy Gray, Angela Bradbury and Daniel Vorhaus, 'Direct-to-Consumer Genetic Testing: Personalized Medicine in Evolution' (2011) *Genomics Law Report* 34-40, 39.

[74] Cecelia Bellcross, Patricia Page and Dana Meaney-Delman, 'Direct-to-Consumer Personal Genome Testing and Cancer Risk Prediction' (2012) 18(4) *The Cancer Journal* 293-302, 294.

[75] See Sigrid Sterckx, Julian Cockbain, Heidi Howard, Isabelle Huys and Pascal Borry, '"Trust is not something you can reclaim easily": patenting in the field of direct-to-consumer genetic testing' (2013) 15(5) *Genetics in Medicine* 382-387.

[76] To illustrate consumer acceptance, Australians spent $A26.5 billion online in the twelve months to June 2018. <https://business.nab.com.au/nab-online-retail-sales-index-june-2018-30746/>. See Pew Research Center, *Health Online 2013* (2013) <http://pewinternet.org/Reports/2013/Health-online.aspx>.

**[77]** See Jennifer Wagner, Jill Cooper, Rene Sterling and Charmaine Royal, 'Tilting at windmills no longer: a data-driven discussion of DTCGT DNA ancestry tests' (2012) 14 *Genetics in Medicine* 586-593, 591.

[78] Jennifer Wagner, 'Interpreting the Implications of DNA Ancestry Tests' (2010) 53(2) *Perspectives in Biology and Medicine* 231-248, 231.

[79] 23andMe, 'Party till you spit' 4 December 2007, <https://blog.23andme.com/news/inside-23andme/party-till-you-spit/>.

frameworks. Disruptive innovations have typically occurred in the commercial sphere and describe the 'process whereby a smaller company with fewer resources is able to successfully challenge established incumbent businesses', by servicing specialised or underserviced consumers or creating markets where none existed.[80] DTCGT represents a disruptive innovation where the impact is felt outside the commercial sphere, with the medical sphere in this case representing the 'established incumbent'. Unlike previous commercial involvement in medicine, DTCGT plays an alternative rather than complementary role, with the services offered directly encroaching and potentially directly competing in areas previously the exclusive purview of medical professionals.

DTCGT is not only disruptive to the medical sphere but also consumers as it represents a discontinuous innovation. Rather than being a modification to existing products or services, DTCGT is a new commercial service offering, requiring cognitive, affective and behavioural changes. DTCGT requires consumers to acquire knowledge about genetics and genetic testing, develop positive attitudes and formulate behavioural intentions pre-purchase. DTCGT's disruptive nature is further compounded by qualities of its offering, those aspects used by consumers to make purchase decisions and ultimately determine satisfaction. As a service, DTCGT is low in both search and experience qualities but high in credence qualities due to its intangible nature. Search qualities refer to aspects that can be determined by inspection pre-purchase (e.g. specific car features) with experience qualities being those aspects only determinable during or after service provision (e.g. quality of haircut). Credence attributes however are difficult to evaluate even after service provision and must be accepted by consumers 'on faith' (e.g. expertise of surgeon). With commercial offerings, consumers often rely on extrinsic aspects in their decision-making, especially those controlled by companies such as marketing messages, seals of approval, accreditation or celebrity endorsers. Relative to DTCGT, the majority of consumers lack the expertise or are not provided with the specialised information necessary to determine the veracity of corporate claims, especially relative to benefits and risks. Actual DNA testing is removed from consumers so they cannot assess the accuracy of either tests or results, and consumers are left to self-interpret provided results.[81]

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[80] Clayton Christensen, Michael Raynor and Rory McDonald, 'What is Disruptive Innovation?' (2015) December *Harvard Business Review* <http//hbr.org/2015/12/what-is-disruptive-innovation>.

[81] For further detail see Jan Charbonneau, Michael Solomon, Greg Marshall and Elnora Stuart, *Marketing: Real People, Real Choices* 2nd ed. (Pearson New Zealand, 2011) Chapter 10 for qualities of the offering and Chapter 6 for innovations.

### 2.3.2 *Empowering consumers: The promise of DTCGT*

*'Science has a reputation of being inaccessible, for the super smart or the elite, but I want to make people realise that science is accessible to everyone and anyone can understand their genome and it is fascinating.'*[82]

It has been suggested DTCGT has a role to play in the 'age of personalised medicine'[83] as it represents 'a powerful mechanism for providing comprehensive genomic information to a large number of individuals',[84] thereby facilitating individual choice and fostering consumer empowerment[85] relative to healthcare and lifestyle decision-making[86] and speeding the 'translation of scientific discovery',[87] without drawing on public resources.

Developments in the DTCGT sector have drawn the attention of not just consumers but academics and medical researchers,[88] media,[89] health-related organisations,[90] and those concerned with

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[82] Anne Wojcicki, CEO 23andMe as reported in Samuel Gibbs, 'DNA-screening test 23andMe launches in UK after US ban' 2 December 2014 *The Guardian* <https://www.theguardian.com/technology/2014/dec/02/google-genetic-testing-23andme-uk-launch>.

[83] See Don Chalmers, Dianne Nicol, Margaret Otlowski and Christine Critchley, 'Personalised Medicine in the Genome Era' (2013) 20(3) *Journal of Law and Medicine* 577-594.

[84] Sancy Leachman, Daniel MacArthur, Misha Angrist, Stacy Gray, Angela Bradbury and Daniel Vorhaus, 'Direct-to-Consumer Genetic Testing: Personalized Medicine in Evolution' (2011) *Genomics Law Report* 34-40. <http://www.genomicslawreport.com/wp-content/uploads/2011/06/ASCO-DTC-Abstract.pdf>.

[85] See Donato Ramani and Chiara Saviane, 'DCGT: the individual's benefits above all' (2011) 10(3) *Journal of Science Communication* C05.

[86] See Morris Foster, John Mulvihill and Richard Sharp, 'Evaluating the utility of personal genomic information' (2009) 11(8) *Genetics in Medicine* 570-574.

[87] Amy McGuire and Wylie Burke, 'Health system implications of direct-to-consumer personal genome testing' (2011) 14 *Public Health Genomics* 53-58, 53.

[88] See Jane Kaye, 'The Regulation of Direct-to-consumer Genetic Tests' (2008) 17 *Human Molecular Genetics* R180-R183; Audrey Chapman, 'DTCGT Marketing of Genetic Tests: The Perfect Storm' (2008) 8 *The American Journal of Bioethics* 10-12; Stuart Hogarth, Gail Javitt and David Melzer, 'The Current Landscape for Direct-to-consumer Genetic Testing: Legal, Ethical and Policy Issues' (2008) 9 *Annual Review of Genomics and Human Genetics* 161-182.

[89] In 2008, Time Magazine awarded its Invention of the Year to 23andMe's DNA-testing service for pioneering retail genomics. Anon, 'Best Inventions of 2008', *Time*, <http://www.time.com/time/specials/packages/article/0,228804,1852747_1854493_1854113,00.html>. See John Lynch, Ashley Parrott, Robert Hopkins and Melanie Myers, 'Media Coverage of Direct-to-consumer Genetic Testing' (2011) 20 *Journal of Genetic Counseling* 486-494.

[90] See Human Genetics Society of Australasia, *Position Statement: Online DNA Testing* (2018) 2018 PSO2 <https://www.hgsa.org.au/documents/item/18>; American College of Medical Genetics and Genomics, 'Direct-to-consumer genetic testing: a revised position statement of the American College of Medical Genetics and Genomics; (2016) 18(2) *Genetics in Medicine* 207-208; Association for Molecular Pathology Position Statement, 'Direct access to genetic testing (Direct-to-consumer genetic testing) (2015) <https://www.amp.org/AMP/assets/File/position-statements/2015/AMPpositionstatementDTCtesting-FINAL_002.pdf>; Australian Government, NHMRC, *Direct-to-consumer genetic testing: A statement from the National Health and Medical Research Council,* (2014) Ref# G9 1-4;; Royal College of Pathologists of Australasia, Position Statement: Genetic tests that are marketed directly to consumers (2013) No. 2

regulation.[91] Much of the early academic literature was 'learned opinion', applying the lens of particular disciplines to the emerging field of DTCGT.[92] Two key themes emerge from the literature: the promise of *consumer empowerment* and the potential for *consumer harm*.

According to DTCGT proponents, individuals have a *right* to the information in their own DNA, and that having the genetic information contained in their DNA leads to *consumer empowerment* – using test information to make informed healthcare and lifestyle decisions. The DTCGT industry itself has always argued individuals have a fundamental right to access information contained in their own DNA – the key words being *access* and *information*. Underlying the concept of the right to access one's own genetic information is the ethical notion of autonomy and self-determination. Relative to health the 'guiding principle should be the individual's right of looking for information, freely selecting the source, in order to take the most appropriate decision'.[93] It has been suggested that 'citizens worldwide have too long a history of being passive players in health care – blindly following instructions from providers.'[94] DTCGT's proponents agree that '… having access to their own personal genomic information can enhance individuals' sense of choice and control, with the knowledge obtained contributing to better patient's outcomes', customising drug selection and dosage, increasing preventative screening or altering primary care management.[95]

The DTCGT industry believes it is 'empowering people to become informed healthcare consumers' and enabling 'individuals to learn about the basics of genetics through the lens of their own data', with test results serving as a 'foundation to preventive care', at an affordable price-point,

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<https://www.rcpa.edu.au/getattachment/2be86825-4c53-4d47-84ec-a2730954b021/Genetic-Tests-that-are-Marketed-Directly-to-Consum.aspx>.

[91] See European Academies Science Advisory Council, Direct-to-consumer genetic testing for health-related purposes in the European Union Policy Report 18 (2012); European Academies Science Advisory Council, A 'Common Framework of Principles' for Direct-to-consumer Genetic Testing Services. Principles and Consultation Questions (2009); Human Genetics Commission, More Genes Direct (2007); Australian Law Reform Commission and Australian Health Ethics Committee, Essentially Yours: The Protection of Human Genetic Information in Australia, Report No 96 (2003); Human Genetics Commission, Genes Direct: Ensuring the Effective Oversight of Genetic Tests Supplied Directly to the Public (2003).

[92] See Timothy Caulfield, 'DTCGT genetic testing: pendulum swings and policy paradoxes' (2012) 81 *Clinical Genetics* 4-6; Timothy Caulfield, (2009) 'Direct-To-Consumer Genetics and Health Policy: A Worst-Case Scenario?' (2009) 9(6-7) *The American Journal of Bioethics* 48-50, DOI: 10.1080/15265160902918770.

[93] Donato Ramani and Chiara Saviane, 'DCGT: the individual's benefits above all' (2011) 10(3) *Journal of Science Communication* C05, 1; Katherine Wasson, 'Consumer alert: Ethical issues raised by the sale of genetic tests directly to consumers' (2008) 8(6) *The American Journal of Bioethics* 16-18.

[94] John Willbanks and Eric Topol, 'Stop the privatization of health data' (2016) 535(7612) *Nature* <https://www.nature.com/news/stop-the-privatization-of-health-data-1.20268>.

[95] Morris Foster, John Mulvihill and Richard Sharp, 'Evaluating the utility of personal genomic information' (2009) 11(8) *Genetics in Medicine* 570-574, 571 and 572.

regardless of geographic location.[96] With DTCGT, individuals do not have to meet CGT criteria, with information generated theirs to determine what it means to them, how to action and with whom to share.[97]

It has been suggested consumers themselves agree. Signatories to non-profit DIYgenomic's petition believed they should have unrestricted access to their genetic information and that healthcare professionals and governments should not function as intermediaries in the DTCGT process.[98] An early study of over 1000 social network users also found over half believed DTCGT increases an individual's control over their health with the majority of those who would consider DTCGT believed results would influence future healthcare decisions.[99]

DTCGT's promise of consumer empowerment by 'democratising' healthcare is difficult to argue against, with even DTCGT's critics acknowledging potential benefits.

### *2.3.3 Realising the promise of DTC: Will consumers purchase?*

*'DTC-PGT will have little social impact if few consumers purchase the genetic tests and act on the results.'*[100]

While figures differ, commercial industry reports suggest a significant market exists for DTCGT and project dramatic growth worldwide. For example, in January 2018 Kalorama Information forecast global sales of US$310 million by 2022, up from US$99 million in 2017 representing annual average growth of 25.6%.[101] By December 2018, Market Insights, Inc. suggested the global market would surpass US$2.5 billion by 2024 – a not insignificant difference.[102] These projections however should be approached with caution as determining veracity is problematic. Projections are generally based on individual companies' provided figures, which are commercially sensitive

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[96] Free State Reporting, Inc., US Department of Health and Human Services, FDA, Molecular and Clinical Genetics Panel, Gaithersburg, Maryland, March 8-9, 2011, 168. Presentation Ashley Gould, General Counsel, 23andMe, Inc.

[97] See Mary-Claire King, Ephrat Levy-Lahad and Amnon Lahad, 'Population-based screening for BRCA1 and BRCA2' (2014) 312(11) *JAMA* DOI: 10.1001/jama.2014.12483.

[98] Yeyang Su, Pascal Borry, Ina Otte and Heidi Howard, "It's our DNA, we deserve the right to test!' A content analysis of a petition for the right to access direct-to-consumer genetic testing' (2013) 10(7) *Personalized Medicine* <https://doi.org/10.2217/pme.13.69>.

[99] Amy McGuire, Christina Diaz, Tao Wang and Susan Hilsenbeck, 'Social Networkers' Attitudes Toward Direct-to-Consumer Personal Genome Testing' (2009) 9(6-7) 3-10.

[100] G Samuel, C Jordens and I Kerridge, 'Direct to consumer personal genome testing: ethical and regulatory issues that arise from wanting to 'know' your DNA' (2010) 40 *Internal Medicine Journal,* 220-224, 222.

[101] PRNewwire Releases 15 January 2018. https://www.prnewswire.com/news-releases/direct-to-consumer-genetic-health-testing-market-to-reach-310-million-says-report-300581607.html>.

[102] PRNewwire Releases 11 December 2018. <https://www.prnewswire.com/news-releases/direct-to-consumer-genetic-testing-market-to-hit-2-5-bn-by-2024-global-market-insights-inc--830436085.html>.

and therefore not independently verifiable. Further, each commercial vendor employs their own forecasting methods e.g. extrapolating US data only. For example, in 2016 Kalorama forecast the US market would reach US$211 million in 2017; significantly lower than 2017 global sales reported in 2018.[103] While quantifying the market may be difficult, these reports suggest consumers seeking greater control over their healthcare and easing of regulatory processes will fuel growth.

Data on the size of the Australian DTCGT market is not available and whether significant growth as forecast would be experienced locally is open to debate and will depend on consumer familiarity and purchase intentions. Product familiarity is 'the cognitive structures of knowledge concerning the product stored in memory … derived from direct or indirect experiences'.[104] While not causally linked to purchase, both familiarity and purchase intention are prerequisites, and within the industry's control to increase through pricing and promotional strategies. Consumer genetics education programmes and mass media reports also serve to increase familiarity within the general public.

Published studies suggest DTCGT familiarity, even in the US market, is generally low with a 2014 Australian study reporting that while 93% of respondents knew such tests were available only 40% believed they were available onshore.[105] Australian research also suggests low purchase intentions, finding Australians significantly less likely to approve of or order DTCGT compared to CGT, with privacy concerns and lack of genetic counselling cited as barriers to uptake.[106] Research investigating onshore versus offshore purchase likelihood confirmed low intention for onshore

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[103] Meghana Kershavan, 'These are the key players in the home health testing market' 20 January 2016 <https://medcitynews.com/2016/01/20-key-players-in-the-direct-to-consumer-lab-testing-market/>.
[104] Larry Marks and Jerry Olson, 'Towards a cognitive structure conceptualization of product familiarity' (1981) (8) *Advances in Consumer Research* 145-150, 145.
[105] Loredana Covolo, Sara Rubinello, Elisabetta Ceretti and Umberto Gelatti, 'Internet-based direct-to-consumer genetic testing: A systematic review' (2015) 17(12) *J Med Internet Res* DOI: 10.2196/jmir.4378; Jacqueline Savard, J Mooney-Somers, Ainsley Newsom and Ian Kerridge, 'Australian's knowledge and perceptions of direct-to-consumer personal genome testing' (2014) 44(1) *Internal Medicine Journal* 27-31.
[106] Sylvia Metcalfe, Chriselle Hickerton, Jacqueline Savard, Bronwyn Terril, Erin Turbitt, Clara Gaff, Kathlene Gray, Anna Middleton, Brenda Wilson and Ainsley Newson, 'Australian's views on personal genomic testing: focus group findings from the Genioz study' (2018) *European Journal of Human Genetics* <https://doi.org/10.1038/s41431-018-0151-1 (7 focus groups of 56 individuals); Jacqueline Savard, J Mooney-Somers, Ainsley Newsom and Ian Kerridge, 'Australian's knowledge and perceptions of direct-to-consumer personal genome testing' (2014) 44(1) *Internal Medicine Journal* 27-31 (Facebook survey of 270 respondents); Christine Critchley, Dianne Nicol, Margaret Otlowski and Don Chalmers, 'Public reaction to direct-to-consumer online genetic tests: Comparing attitudes, trust and intentions across commercial and conventional providers' (2014) *Public Understanding of Science* DOI: 10.1177/0963662513519937 (Computer assisted telephone interviewing (CATI) of 1000 Australians).

purchase, with intention dropping even further for offshore companies.[107] However, it also found purchase likelihood however was influenced by both illness severity and clinical utility, with likelihood highest for life-threatening conditions with available treatment, suggesting severity and clinical utility function as potential triggers for uptake.[108] Interest has also been shown to increase if individuals felt they would regret not taking the test, could learn about children's risk, and if communication was evidence-based however providing risk information decreased interest.[109]

If, as expected, more companies enter the Australian DTCGT marketplace and marketspace, it would be expected that Australian familiarity levels would increase.[110] Given Australian attitudes are relatively positive to both genomic research and development of genetic technologies, if familiarity and purchase intentions increase, DTCGT demand will also likely increase.[111]

## CONCLUSION

This chapter provides context for the evidence-based component of this research, investigating how Internet-literate members of the general public engage with DTCGT and the flow-on psychological and behavioural responses.

Part One provided an overview of genetics, explaining how human characteristics are inherited, how genetic variations occur and the role of mutations, particularly SNPs, in disease development. It is important to contrast monogenic diseases where single gene mutations result in diseases such as Cystic Fibrosis and genetic tests are definitive with the far more common

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[107] Gordana Bruce and Christine Critchley (2013) *Swinburne National Technology and Science Monitor* <http://apo.org.au/system/files/119126/apo-nid119126-477751.pdf>. CATI survey of 1000 Australians. Purchase likelihood questions by Jan Charbonneau.

[108] See also Nola Ries, Robin Hyde-Lay and Timothy Caulfield, 'Willingness to pay for genetic testing: A study of attitudes in a Canadian population' (2010) 13 *Public Health Genomics* 292-300.

[109] Saskia Sanderson and J Wardle, 'Associations between anticipated reactions to genetic test results and interest in genetic testing: will self-selection reduce the potential for harm?' (2008) 12(1) *Genet Test* 59–66; K Tercyak, A Hensley, K Emmons, I Lipkus, B Wilfond and C McBride, 'Parents' attitudes toward pediatric genetic testing for common disease risk' (2011) 127(5) *Pediatrics* e1288-1295.

[110] Marketspace refers to the online environment and requires no in-country corporate presence or registration.

[111] Gordana Bruce and Christine Critchley, 2013 Swinburne Monitor, Swinburne University of Technology <http://apo.org.au/system/files/119126/apo-nid119126-477751.pdf>. See also Lidewij Henneman, Eric Vermeulen, Carla van El, Liesbeth Claassen, Danielle Timmermans and Martina Cornel, 'Public attitudes towards genetic testing revisited: comparing opinions between 2002 and 2010' (2012) *European Journal of Human Genetics* 1-7; Benjamin Bates, John Lynch, Jennifer Bevan and Celeste Condit, 'Warranted concerns, warranted outlooks: a focus group study of public understandings of genetic research' (2005) 60 *Social Science & Medicine* 331-344.

polygenic and multi-factorial diseases. Polygenic diseases involve two or more genes while multi-factorial diseases not only involve multiple genes but also environmental factors resulting in complex diseases such as cancer and diabetes. Tests for these diseases are not definitive but rather indicate an increased or decreased susceptibility – relative risk − compared to reference populations. Add into the mix environmental factors, and the role played by chance through random replication errors suggested in emerging research and the complexity increases, even for those trained in genetics. The visuals in Appendix One illustrate to both experts and lay people alike just how complex human genetics is when you realise the tiny nucleus in Figure 1.2 contains *all* of the information contained in *all* of the volumes in Figure 1.1.

While individuals armed with DTCGT results would not be expected to have in-depth genetics knowledge, there are key aspects that are necessary, at minimum, to interpret and contextualise results. Individuals must appreciate DTCGT results provide genetic information only and these results are very much constrained by the scientific knowledge of the day as tests analyse SNPs currently believed to be associated with diseases. Most SNPs currently in use are only weakly associated requiring interaction with other genetic or environmental factors, both known and unknown, for diseases to present.[112] However, susceptibility does not mean inevitability, so individuals must consider DTCGT results in the context of environmental factors such as personal lifestyle and appreciate results provide no information about onset, symptoms or severity or importantly, how to mitigate risk.

Part Two illustrates how science and technology operate hand in hand with advances in one leading to advances in the other. Each of the key genetic discoveries and technology advances discussed in this part were necessary to create the environment for DTCGT to gain a foothold. This part also illustrates how commercial involvement has increasingly run parallel to these discoveries, creating the tension that has long existed between public and commercial science. Given the accelerating rate of genetic discoveries and technology advances, it is expected commercial involvement in the business of genetics and in particular DTCGT will also increase.[113]

Part Three briefly discusses both the controversy and promise of DTCGT. As a disruptive innovation, DTCGT was always going to create controversy, especially as it challenges the traditional medical paradigm of CGT. While commercialisation in genetics is not new, DTCGT

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[112] Bridget Kuehn, 'Risks and Benefits of Direct-to-Consumer Genetic Testing Remain Unclear' (2008) 300(13) *JAMA* 1503, 1503.
[113] Antonio Regalado, '2017 was the year consumer DNA testing blew up' 12 February 2018, *Technology Review* <https://www.technologyreview.com/s/610233>.

presents particular challenges to the medical community who previously had exclusive purview over genetic testing, and to consumers who are faced with a new option. The promise offered by DTCGT, much like Collins' 'brave new world' is seductive. It is difficult to argue against empowered consumers armed with their own genetic information becoming active participants in their own healthcare decisions or taking control of their own health by engaging in proactive mitigation strategies. However even Collins queried '... whether access to this kind of information about risk will actually empower individuals to make changes in their healthcare behaviour ... or whether this will be primarily a recreational experience with no long-term consequences.'[114]

As consumer demand increased from the mid 2000s, questions have been raised about the potential for consumer detriment or harm, especially psychological detriment, resulting from the rapid translation of genetic discoveries into for-profit tests and whether consumers will actually use DTCGT results to improve their health.[115] These concerns remain on point given forecasts for increased growth in DTCGT as consumer detriment, if it exists, is a consequence of purchase.

Whether DTCGT is 'empowering or endangering the pubic' remains the big question to be answered.[116] The next chapter investigates the processes and protections afforded individuals in both CGT and DTCGT while the following chapter outlines the key concerns expressed in the literature used to inform the empirical component of this research.

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[114] Francis Collins, *The Language of Life* (Harper, 2010), 88.
[115] Organisation for Economic Co-operation and Development, *Consumer Policy Toolkit*, 2010, <http://www.oecd.org>.
[116] Jennifer Wagner, 'Interpreting the Implications of DNA Ancestry Tests' (2010) 53(2) *Perspectives in Biology and Medicine* 231-248, 245. See also Gail Javitt, 'Direct-to-consumer genetic testing: Empowering or endangering the public?' <http://www.dnapolicy.org/images/issuebriefpdfs/2006_DTCGT_Issue_Brief.pdf>.

# Chapter Three:

# Pathways, processes and protections:

# Australia's DTCGT and CGT spaces

# INTRODUCTION

A solid understanding of the space and its key players and gatekeepers is fundamental to conducting a critical evaluation of existing regulation or developing *sui generis* regulation in any sector. However, 'in order to understand regulation, attention must be paid to the physical places where regulation occurs' – the *regulatory space*.[1] This chapter serves to provide insight into both Australia's CGT and DTCGT spaces, through a combination of doctrinal research and empirical modelling, applying both law and consumer behaviour lens.

Traditionally, genetic testing has been the exclusive purview of medical professionals, with access tightly controlled and results expertly interpreted and actioned. With the advent of DTCGT, individuals seeking genetic information whether to satiate curiosity or in response to familial or personal health-related concerns, can now 'spit in a tube', pay a comparatively small fee and receive what the industry represents as a 'treasure chest' of genetic information. DTCGT's proponents exhort the benefits of opening the treasure chest, revealing genetic information that can be used by individuals in health and lifestyle decision-making. DTCGT's critics urge caution, suggesting the treasure chest may in fact be Pandora's Box, with the potential to generate more harm than good. Whomever is ultimately proven correct, DTCGT represents a paradigm shift from *medical* to *consumer*, with new players entering the genetic testing space, presenting challenges to regulators, healthcare professionals and individuals. This six-part chapter explores available pathways to health-related genetic testing, the key processes involved from both a sector and individual perspective, and the protections afforded individuals depending on the pathway selected.

Part One introduces the two pathways to health-related genetic testing and the roles played by individuals pursuing each – CGT where the individual is legally deemed a *patient* and DTCGT where the individual is legally deemed a *consumer*. As this research focuses on Australia with the US as a comparative, an overview of both healthcare systems is provided as these provide the environment within which CGT occurs.

Part Two models the CGT and DTCGT spaces from both a sector-wide and individual perspective, presenting results graphically. The modelling exercise identifies that the initial bifurcated system of pathways can merge either as the result of company-initiated or consumer-initiated

[1] Samuel Taylor-Alexander, Edward Dove, Isabel Fletcher, Agomoni Ganguli Mitra, Catriona McMillan and Graeme Laurie, 'Beyond regulatory compression: Confronting the liminal spaces in health research regulation' (2016) 8(2) *Law, Innovation and Technology* 149-176, 151. Noting the 1989 work of Leigh Hancher and Michael Moran.

engagement with healthcare. Modelling also identifies key DTCGT flow-on effects as individuals armed with genetic information begin sharing with family or online. While the same basic steps are involved in the CGT and DTCGT processes from an individual's perspective, modelling reveals significant differences, especially relative to needs assessment and results interpretation.

Part Three discusses the medical, quality and financial gatekeepers involved in the CGT process and describes how each gatekeeper provides protection for *patients*, such as the duty of care owed them by medical and genetic professionals. Gatekeepers such as Medicare and the Therapeutic Goods Administration (TGA) ensure genetic tests are valid with Medicare as well as state and territory Health Departments determining which are available and subsidised. The National Association of Testing Authorities ensures laboratories conducting genetic tests adhere to international standards so that results provided to medical professionals are valid.

Part Four outlines the protections afforded DTCGT *consumers* by the TGA and Australian Consumer Law (ACL), as administered by the Australian Competition and Consumer Commission (ACCC). Part Four also reviews the limited enforcement efforts in Australia and also in the US, where both regulators and the courts have been more active in the DTCGT space. Given similar regulatory structures, both US regulatory actions and court decisions provide insight for Australian regulators.

Part Five introduces a new role for individuals – that of *research participant*. Individuals wishing to participate in medical research now have an additional pathway to the traditional medical research of clinical trials by allowing their genetic specimens and data to be used in DTCGT corporate research.

Part Six addresses the guidance provided by the *Consumer Policy Toolkit* (CPT) in determining whether specific consumer protection is needed for DTCGT *consumers*. The six-step approach outlined in the CPT revolves around determining and quantifying consumer detriment − the focus of the survey component of this research.

## PART ONE: PATHWAYS TO HEALTH-RELATED GENETIC TESTING

Individuals seeking health-related genetic information in response to symptoms or family history have traditionally had one pathway for access to CGT – through healthcare practitioners within each country's healthcare system. When individuals engage with health-related genetic testing through this pathway, they enter the medical sphere as a *patient*, afforded all rights, responsibilities and protections this designation entails. For the purposes of this research, a *patient* is a person receiving medical care from a licensed healthcare practitioner, including diagnosis and providing treatment.[2]

CGT access is only provided for testing deemed 'clinically relevant' by qualified healthcare providers.[3] In Australia, clinically relevant services are those generally accepted by the medical profession as necessary for appropriate patient treatment.[4] A more detailed definition is used in the US with medically necessary services those needed to 'treat an illness, injury, condition, disease, or its symptoms and that meet accepted standards of medicine'.[5] Both definitions focus on consensus of expert opinion, with healthcare professionals viewing CGT through the lens of clinical utility, undertaking CGT only if tests have predictive value and/or can inform proven medical care options.

The emergence of DTCGT has provided an alternative pathway for individuals to bypass healthcare gatekeepers, accessing health-related genetic information 'at the click of a mouse'. Individuals engaging with health-related genetic testing through this pathway enter the commercial sphere as a *consumer*, again afforded all the rights, responsibilities and protections this designation entails. In Australia, a *consumer* is person acquiring goods or services of a kind

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[2] As there is lack of agreement on the precise meaning, various components from multiple definitions were incorporated into this definition. See <https://medical-dictionary.thefreedictionary.com>, <https//www.medicinenet.com>; Amy McGuire and Wylie Burke, 'Health system implications of direct-to-consumer personal genome testing' (2011) 14 *Public Health Genomics* 53-58. Increasingly patients are being referred to as 'health consumers' but this term is not used to avoid confusion.

[3] 'Medical tourism' where individuals travel outside their country for CGT and medical/pharmaceutical interventions is beyond the scope of this research.

[4] Medicare Benefits Schedule, Department of Health, Australian Government. <http://www.health.gov.au/internet/hta/publishing.nsf/content/mbs-1>. See also Medical Board of Australia, *Good Medical Practice: A Code of Conduct for Doctors in Australia* March 2014 <https://www.medicalboard.gov.au/codes-guidelines-policies/code-of-conduct.aspx>.

[5] Medicare Glossary, Medicare.gov, US Government <https://www.medicare.gov/glossary/m

ordinarily acquired for personal, domestic or household use or consumption under the value of $40,000.[6]

Research has suggested individuals engage with DTCGT for a range of reasons. Some seek DTCGT to gain medically relevant information such as personal disease risk or carrier status in response to personal or familial symptoms and concerns, some because the information is potentially embarrassing or they have privacy or insurance concerns, while others are simply curious about their genetic makeup.[7] Some seek information that is simply not available via CGT. Individuals may also be gifted DTCGT kits, with the industry heavily promoting kits at holiday times.[8] Further, companies offering bundled tests including DTCGT, ancestry and traits appeal to an even broader range of motivations.

While two separate pathways exist, individuals are not precluded from pursuing both, depending on their particular motivations and situations. The following two sections look at the environment within which each pathway operates, providing both background and context for the processes undertaken and protections afforded.

### *3.1.1 CGT: Doctors and patients in the clinic*

#### *3.1.1.1 Australia's healthcare system*

CGT operates wholly within Australia's healthcare system, a complex system with combined federal and state/territory responsibility. *The Commonwealth of Australia Constitution Act 1900* (Cth) s51(ii) vests revenue-raising authority solely in the federal government, but not healthcare which defaults to individual states and territories. The federal government has however been provided authority for pharmaceutical and medical services amongst others through the

[6] *Competition and Consumer Act 2010* (Cth), sch 2 ('Australian Consumer Law'). A full definition is provided in Schedule 2, s3.

[7] See Sarah Gollust, E Gordon, C Zayac, G Griffin, M Christman, R Pyeritz, L Wawak and B Bernhardt, 'Motivations and Perceptions of Early Adopters of Personalized Genomics: Perspectives from Research Participants' (2012) 15 *Public Health Genomics* 22-30; Yeyang Su, Heidi Howard and Pascal Borry, 'Users' motivations to purchase direct to consumer genome-wide testing: an exploratory study of personal stories' (2011) 2 *J Community Genet* 135-146; Michelle McGowan, Jennifer Fishman and Marcie Lambrix, 'Personal genomics and individual identifies: motivations and moral imperatives of early adopters' (2010) 29(3) *New Genet Soc* 261-290.

[8] See <https://www.usmagazine.com/shop-with-us/news/23andme-ancestry-kits-last-minute-gift/>.

*Constitution Alteration (Social Services) 1946* (Cth) s51(xxiiiA), while states and territories retain control over public hospitals, funded by federal transfer payments.[9]

Three levels of government share responsibility for healthcare: federal, state/territory, and local. The Commonwealth government takes a leadership role in policy making and research. State and territory governments bear primary responsibility for the delivery and management of public sector health services and maintain direct relationships with health care providers. Local governments focus primarily on public health initiatives. The Council of Australian Governments (COAG) allows for Commonwealth, state, and territory governments to co-ordinate efforts or transfer state and territory powers to the Commonwealth.[10] For example, in August 2011, under the COAG National Health Reform Agreement Commonwealth and state/territory governments became jointly responsible for funding public hospital services and establishing nationally consistent health standards amongst others.

Healthcare is costly and expected to continue rising, with Australia spending AU$180.7 billion in 2016-17 or AU$7400 per capita, up from AU$7100 in 2015-16. Healthcare is funded primarily from federal, state and territorial government subsidisation, with the remainder from private health insurance, personal contributions and other non-governmental sources.[11]

### *Government subsidisation: universal access*

Consistent with Australia's view of healthcare as public good and therefore a public responsibility, since 1984 Medicare has provided *universal* access to public hospitals, registered primary healthcare professionals, required tests and drugs for citizens, permanent residents and those from countries with reciprocal health agreements.[12] Medicare is funded through compulsory levies on taxable income, administered federally through the Department of Human Services and has three key components − hospital, medical and pharmaceutical. Subsidisation for eligible *clinically relevant services* is detailed in the Medicare Benefits Schedule (MBS) and eligible pharmaceuticals in the Pharmaceutical Benefit Scheme (PBS). Practitioners can choose to accept

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[9] See Australian Government Australian Institute of Health and Welfare, *Health Expenditure Australia 2011-12* (2013), 3 for a useful chart outlining the flow of funds. <http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=60129544656>.

[10] See National Healthcare Agreement 2012 detailing responsibilities of Commonwealth, State and Territorial governments <http://www.federalfinancialrelations.gov.au/content/npa/healthcare/national-agreement.pdf>.

[11] Australian Government, Australian Institute of Health and Welfare, *Health Expenditure Australia 2016 – 17* (2018) <https://www.aihw.gov.au/reports/health-welfare-expenditure/health-expenditure-australia-2016-17/formats>; Australian Institute of Health and Welfare, *Australia's Health 2018: In brief* (2018) Cat. no AUS201, Canberra, AIHW, 39.

[12] *Health Insurance Act 1973* Part I s3 for definition of 'registered primary healthcare professional'.

Medicare benefits only or charge higher fees, with the difference funded by either private health insurance or personal contributions. Medicare has safety-net provisions capping patients' yearly 'out-of-pocket' costs.

### *The role of private health insurance*

In 1997, the Commonwealth actively encouraged development of a strong private health insurance sector, enacting a regulatory framework to encourage uptake by Australian citizens.[13] Private health insurance is regulated by the *Private Insurance Act 2007* (Cth) and provides subsidised access to private hospitals including choice of doctor, and allied healthcare such as dental if individuals so choose. Private health insurance is community-rated, meaning premiums and benefits are based on specific cover selected not criteria such as health status – individuals do not have to declare health status or undergo medical examinations prior to or during coverage periods.[14] Life, income protection and disability insurance however are risk-rated, requiring declaration of health status, including known genetic conditions for determination of coverage and rates.

Private insurance companies themselves decide on specific coverage packages and fees, waiting periods and reimbursement levels. Fees increase annually with the overall industry percentage increase requiring government approval. To encourage uptake, the Commonwealth government provides income and age-tested rebates on premiums and imposes additional surcharges on non-privately insured high-income earners.[15] As at December 2017, 45.6% of Australians had private hospital and 54.6% allied healthcare cover.[16]

### *Health system performance*

Australia performs reasonably well on OECD quality care measures such as mortality and survival rates and has higher than average life expectancy at 82.5 years, suggesting effective system performance.[17] Risk factors such as rising obesity rates and obesity's link with illnesses such as Type 2 Diabetes are noted however as of concern for future system performance. For example, in

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[13] See Fiona McDonald and Stephen Duckett, 'Regulation, private health insurance and the Australian health system' (2017) 11(1) *McGill Journal of Law and Health* S31-S60.
[14] *Private Insurance Act 2007* (Cth) s55-5(2).
[15] See *Private Insurance Act 2007* (Cth) Divisions 2 and 3.
[16] Australian Prudential Regulation Authority <https://www.apra.gov.au/publications/private-health-insurance-membership-and-benefits>.
[17] Organisation for Economic Co-operation and Development, 'Health at a Glance 2017: OECD Indicators How does Australia compare?' (2017) <www.oecd.org/health/health-at-a-glance.htm>.

2016-2017, 70% of adult males, 56% of adult females and, concerningly, 28% of children aged 5-17 were overweight or obese.[18]

### *3.1.1.2 United States' healthcare system*

While the primary focus of this chapter, and indeed this research, is Australia, it is important to provide an overview of the US healthcare system for both contrast and context for empirical results presented in Chapter Six.[19] Perhaps the key difference between the two systems is philosophical, with the US viewing healthcare more as a private good and therefore private (read commercial) responsibility.

Like Australia, the American healthcare system is complex, combining federal and state responsibility, with funding derived from a combination of government subsidisation, private health insurance and personal contributions. The United States Constitution does not provide explicit rights to healthcare, requiring Congress to use its Article 1 section 8, general welfare and taxation powers, to provide healthcare to specific groups and its interstate commerce power to regulate private health insurance.[20] Many states, however, do have constitutional powers over, and jointly fund, healthcare, resulting in healthcare provision varying by state.[21]

The US has the highest healthcare expenditure of all OECD countries, spending US$3.3 trillion in 2016 equating to US$10,348 per capita.[22] Table 3.1.1 provides direct comparisons of per capita health spend between AU and US as well as forecasts indicating increases in both countries. While similarities exist, the two countries approach healthcare policy from different perspectives. The US favours limited public intervention, allowing the bulk of healthcare to be subject to free market forces. This is best illustrated by comparing funding proportions. In 2014, 70% of Australian healthcare was funded by government subsidisation, 10% private insurance and 20% personal contributions compared with 50%, 39% and 11% respectively for the US.[23]

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[18] Australian Institute of Health and Welfare, *Australia's Health 2018: In brief* (2018) Cat. no AUS201, Canberra, AIHW, 17.
[19] Substantive reporting or analysis of other jurisdictions is beyond the scope of this research.
[20] Constitution of the United States <https://www.archives.gov/founding-docs/constitution-transcript>.
[21] See Kathlene Swendman, 'Health care: Constitutional rights and legislative powers', Congressional Research Service Report 7-5700, July 9, 2012.
[22] Centers for Medicare and Medicate Services, *NHE Fact Sheet* <http://www.cms.gov/research>.
[23] Global Burden of Disease Health Financing Collaborator Network, 'Evolution and patterns of global health financing 1995 – 2014: development assistance for health, and government, prepaid private, and out-of-pocket health spending in 184 countries' (2017) 389 *The Lancet* 1981-2004, 1985. Latest available direct comparisons also used in Table 3.1.1.

**Table 3.1. Per capita healthcare spend: Australia and United States.**

| Per capita healthcare spend | Country | |
|---|---|---|
| $US | AU | US |
| 2014 | $4032[1] | $9237[2] |
| 2030 | $5606 | $12448 |
| 2040 | $6970 | $15026 |

[1] 9% of GDP *cf.* 3.3% in 1995. [2] 16.6% of GDP *cf.* 2.9% in 1995.

### *Government subsidisation: selective access*

Since 1965, Medicare has provided *selective* access to healthcare for US citizens and permanent residents aged 65+ and those with severe disability, regardless of income, as well as designated groups such as serving military. Medicare is a federal program funded jointly by payroll taxes and Congressional allocation. Unlike Australia where clinical relevance is determined by the healthcare profession, in the US, what is deemed medically necessary, and therefore covered, is determined largely by federal and state laws and decisions by local companies processing medical claims.[24] Qualifying individuals select either Medicare Original with restricted free coverage, or extend coverage through privately funded health insurance. Medicaid provides healthcare for those on lower incomes, a jointly funded federal and state initiative with eligibility and coverage varying by state.

### *The role of private health insurance*

As Medicare covers approximately 14% of the population and Medicaid 20%, the majority rely on private health insurance, obtained personally or through employers. Health insurance obtained personally is generally more expensive than that obtained through employer plans. Part-time employees and the self-employed however must self-fund, as employee health insurance is generally available to full-time employees only. In 2016, 91.2% of Americans had private health insurance.[25]

Unlike Australia's community-rating, the US health insurance industry is driven by competitive market forces where prices and coverage are risk-rated, considering both current and future health status, including genetic status, with mandatory medical examinations. Risk rating is promoted as providing optimal value, shifting costs from those with lowest to those with highest risks.[26] The federal *Patient Protection and Affordable Care Act* was enacted in 2010 to increase

[24] See <https://www.medicare.gov/what-medicare-covers/>.
[25] Jessica Barnett and Edward Berchuk, *Health Insurance Coverage in the United States 2016* (2017) Reports P60-260 <https://www.census.gov/library/publications/2017/demo/p60-260.html>.
[26] See Donald Light, 'The practice and ethics of risk-rated health insurance' (2012) 267(18) *JAMA* 2503-2508.

private insurance access and affordability. The Act, referred to as Obamacare after Democratic President Obama, extended coverage to pre-existing conditions and aimed to control escalating Medicare costs, specifically targeting low-income households.[27] It remains a hotly contested issue as replacing it is a cornerstone policy of Republican President Trump.

#### *Health system performance*

The United States does not perform as well as Australia on OECD quality care measures. With the highest level of obesity at 88% of adults, lower than average life expectancy at 78.8 years, and delivering only average performance, its healthcare system does not achieve outcomes commensurate with investment.[28]

### *3.1.2 DTCGT: Out of the clinic and into the Cloud*

DTCGT operates within each country's commercial space as well as the online environment. Companies typically conduct marketing activities and return results online, consistent with established e-commerce models where traditional intermediaries such as retailers are eliminated and transactions are completed online. As Internet penetration has increased, consumers have demonstrated increasing acceptance of e-commerce. For example, in 2017 87% of Australians were online and in the 12 months to July 2018 spent approximately AU$27 billion online representing 8.5% of total retail spending.[29] While a country's offline commercial space clearly falls within their jurisdiction, the online environment presents particular challenges as jurisdiction is determined by country of registration, denoted by URL extension. For example, URLs ending with.com.au fall within Australian jurisdiction while those ending with .com fall within US jurisdiction, subject to each country's applicable body of commercial and consumer legislation and regulations.

DTCGT companies have also capitalised on the 'tectonic shift in the ways in which patients consume health and medical information …'[30] with increasing use of online health-related information and self-diagnosis tools, with those searching excessively now referred to as

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[27] See Barack Obama, 'United States health care reform progress to date and next steps' (2016) 316(5) *JAMA* 525-532.
[28] See Organisation for Economic Co-operation and Development, 'Health at a Glance 2017: OECD Indicators How does the United States compare?' (2017) <www.oecd.org/health/health-at-a-glance.htm>.
[29] Anon, 'Active internet users as a percentage of the total population in Australia from 2015 to 2018', <www.statista.com/statistics/680142/Australia-internet-penetration>; nab Online Retail Sales Index <https://business.nab.com.au/nab-online-retail-sales-index>.
[30] Bradford Hesse, David Nelson, Gary Kreps, Robert Croyle, Neeraj Arora, Barbara Rimmer and Kasisomayajula Viswanath, 'Trust and sources of health information' (2005) 165 *Arch Intern Med* 2618-2624, 2618.

'cyberchondriacs'.[31] For example, in 2017, Google found approximately 20% of all searches were health-related, prompting it to add a new function providing standardised expert vetted information for over 900 commonly searched conditions.[32]

# PART TWO: DTCGT AND CGT PROCESSES

Part Two looks at the stages involved in both DTCGT and CGT both from the perspective of the sector and then the individual involved. The DTCGT sector is discussed first, including details of the modelling exercise conducted, then CGT. This part ends with a comparison of the processes from an individual perspective in both the DTCGT and CGT spaces.

The DTCGT sector graphic charting the flow of test kits, DNA samples, results, and advice was the result of the modelling exercise. The flowchart of an individual's engagement with DTCGT was developed after the modelling exercise and discussions with a consenting adult who purchased DTCGT tests from US 23andMe and Australian EasyDNA.

Doctrinal analysis of applicable legislation, regulations and industry standards resulted in the CGT sector graphic charting the flow of DNA samples, results, and advice. The flowchart of an individual's engagement with CGT was developed after discussions with a consenting primary care physician.[33]

## *3.2.1 DTCGT: Modelling the space*

In 2009 and 2011, the US Genetics & Policy Center developed a list of DTCGT companies offering testing for at least one medical condition, pharmacogenomic and/or nutrigenomic test to US consumers either onshore or online.[34] For the purposes of this research, in July 2013 and June 2014, this exercise was replicated and extended for the Australian market to map Australia's DTCGT space.[35] The purpose was not to produce a comprehensive list but rather to investigate the

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[31] See Emily Doherty-Torstrick, Kate Walton and Brian Fallon, 'Cyberchondria: Parsing health anxiety from online behaviour' (2016) 57(4) *Psychosomatics* 390-400; Eoin McElroy and Mark Shevlin, 'The development and initial validation of the cyberchondria severity scale' (2014) 28 *Journal of Anxiety Disorders* 259-265.
[32] Anon, 'Dr Google will see you now: Google launches self-diagnosis search', 1 February 2017, <http://www.abc.net.ay/triplej/programs/hack/dr-google-will-see-you-now/8229078>.
[33] Both individuals provided signed consent after reading required Information Sheets and were provided the option to not be named, which each selected.
[34] Genetics & Public Policy Center, 'GPPC releases updated list of DTC genetic testing companies' (2011). US company and test list, methodology employed, and key words used in Google searches available from researcher as links no longer operational.
[35] Compilation assistance Alex Haddad, Centre for Law & Genetics.

different options available for Australian consumers wishing to purchase DTCGT and develop a richer picture of the space to include how consumers engage with results.[36]

The ten keywords used in the US list were searched both individually and with 'Australia' added (e.g. direct-to-consumer genetic tests/Australia). An additional 26 keywords were searched individually and with the addition of the term 'Australia' to reflect terminology appearing in government reports, academic literature and media (e.g. at-home cancer test/Australia). Website analysis included printing key sections, applying a coding frame including terms of service and privacy policies amongst others, and categorisation of companies.

Comparison of 2013 and 2014 results suggested an industry experiencing growing pains, with new entrants, evolving business models, and companies exiting the space. The focus was on Australia, however modelling also provided insight into the DTCGT space in general. While now well established, at the time several of the business models were just emerging. Most companies identified employed standard e-commerce strategies handling marketing, test kit distribution, service transactions and online results return themselves. It was also noted that several DTCGTs as well as others such as other DNA testing companies (e.g. ancestry) also provided consumers with their raw data files in addition to results reports.

Several added in multi-channel options such as marketing and test kit distribution through shopping sites such as Amazon.com and Ebay.com.au or through 'affiliates' (e.g. wellness centers) and 'accredited' allied professionals (e.g. nutritionists). The process for affiliation or accreditation varied from fee for service to training in results interpretation, with some DTCGTs returning results via this channel. At the time, DTCGT whole genome sequencing companies also began appearing (generally providing raw data only), and in 2015 UK retail pharmacy chain Superdrug became the first to sell DTCGT tests 'over the counter' when it began selling 23andMe tests in its 600 outlets, an option now seen in Australia for pharmacogenomic and nutrigenomic tests.

Figure 3.1 charts the flow of test kits, DNA samples, results, and advice in the standard DTCGT e-commerce model. The DTCGT e-commerce model operates totally within the commercial sphere, subject to applicable legislation, regulation and each country's legal system.

[36] For a comprehensive listing of DTC companies and the services they provide spanning the years 2011 – 2018 see Andelka Phillips, 'Data on direct-to-Consumer Genetic Testing and DNA testing companies', 19th February 2018, DOI: 10.5281/zenodo.117922.

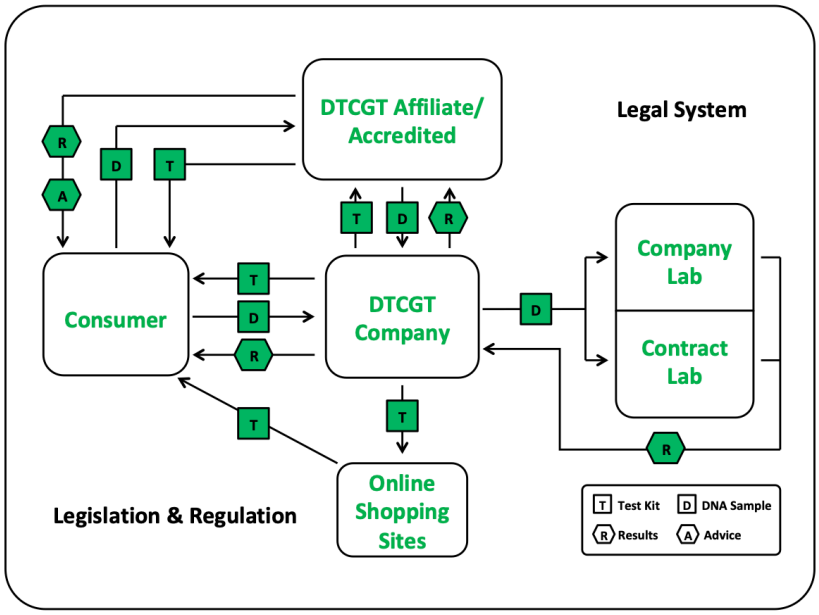


**Figure 3.1 DTCGT: E-commerce model**

Review revealed online shopping sites function simply as distributors of test kit, extending DTCGT's reach to international consumers. The role of affiliates and accredited providers varied with some returning and providing analysis of results and others functioning simply as test kit providers or submitting DNA samples. Either way, these intermediaries interject personal selling into the process and 'muddy the waters', making it difficult to determine when and with whom contractual relationships are formed. It is also significant these intermediaries are the only ones who potentially could provide consumers with advice e.g. results interpretation and intervention suggestions. This aspect is notably absent with DTCGT companies who make it clear results are provided for 'research, education and information only'.

Consumers provide DNA samples in unknown environments as they literally 'spit in a tube' wherever they choose. Of particular interest was the processing of DNA samples. Some companies declared use of their own labs while others contracted this function to independent labs. Some clearly mentioned labs used were accredited, providing accreditation details while others did not. What couldn't be clearly determined however was what happened to DNA samples, whether they were stored, destroyed or returned to DTCGT companies. Even if terms and conditions stated samples were destroyed, individuals were not able to verify. If samples are stored either by labs or DTCGTs, these become 'defacto biobanks', allowing for future corporate use.

### 3.2.2 CGT: Modelling the space

Figure 3.2 charts the flow of DNA samples, results, and advice for CGT offered in Australia's healthcare system. The CGT model operates totally within the medical sphere, subject to applicable legislation, regulation and each country's legal system.

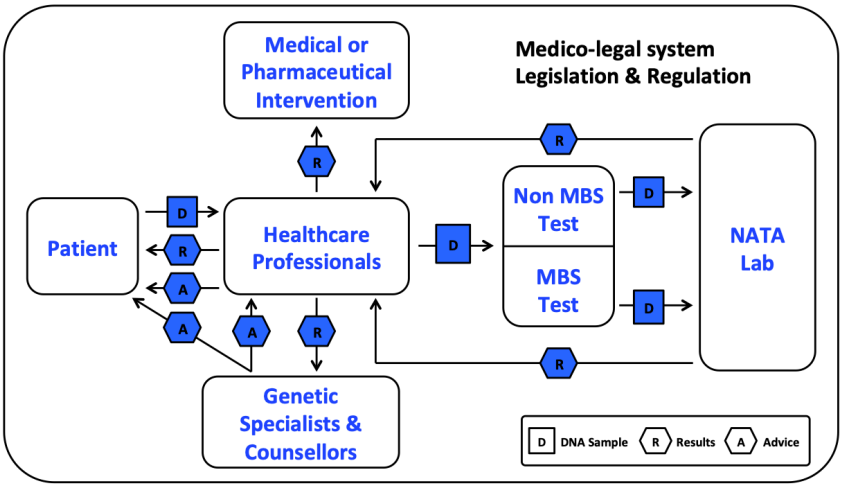


**Figure 3.2 CGT in Australia's healthcare system**

With CGT, tests are ordered by healthcare professionals if deemed warranted, with payment either coming from Medicare, state/territory funding as is most common, or patient contributions. DNA sample provision is either done in clinic or in an accredited laboratory, ensuring patient identification verification, proper labelling of samples, and sterile environments. DNA samples are provided to accredited labs that return results to originating healthcare professionals. Results interpretation is conducted by healthcare professionals and interventions developed, with the assistance of genetic professionals if required. Healthcare professionals *then* discuss results, advice and possible interventions with patients, calling on genetics specialists if required. Medical or pharmaceutical interventions consented to by patients are then arranged, involving medical specialists as required.

### 3.2.3 When DTCGT & CGT pathways cross: Medical and consumer spheres intersect

Figures 3.1 and 3.2 represent two separate spaces, each with its own particular sets of processes and protections. Significantly, analysis of the DTCGT space and flow-on effects identified the potential for engagement between the commercial and medical sphere, suggesting the initial paradigm shift (medical to consumer) may in reality be a paradigm merge (consumer/medical). Two forms of DTCGT engagement were identified: one selected by companies as their business

model, and the other by consumers as their choice. These are presented in Figure 3.3 with aspects occurring in the commercial space in green and those in the medical space in blue.

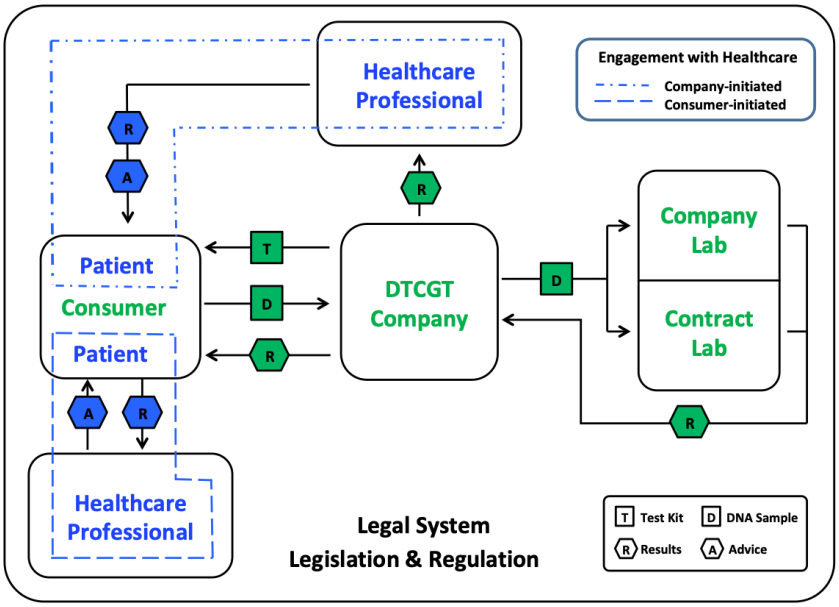


**Figure 3.3 Company and consumer-initiated engagement with healthcare professionals**

Companies such as Myriad Genetics have long engaged with healthcare professionals however this has been entirely within the medical sphere as their tests could only be ordered by physicians. With company-initiated engagement, marketing is conducted directly with consumers but test ordering and/or results return is via individuals' healthcare professionals or via corporate doctors. What was unclear was whether the consent of individuals' personal physicians to participate was obtained prior to results return and whether this effectively transfers liability to physicians. Some companies bypass involvement of individuals' personal physicians, instead offering to select doctors and obtain sign-off once consumers have purchased tests. Consumers have limited, if any, interaction with 'corporate' doctors, and it is unclear in what instances these 'paid for service' doctors would reject sign-off.

With company-initiated interaction, *consumers* are 'forced' to engage with physicians if they wish to receive the results they paid for, and physicians are 'forced' to provide *patients* with results from tests they may be unfamiliar with, or question their validity and utility. It must be noted that

while this business model appears to be gaining some traction in the US, most DTCGTs have adopted traditional e-commerce models.[37]

As such, engagement with healthcare is more typically consumer-initiated interaction, with individuals taking DTCGT results to physicians for confirmation, interpretation assistance, intervention recommendations or psychosocial support, again passing the burden to the healthcare system. Coupled with the DTCGT disclaimer of results being for 'research, education and information only' is usually the recommendation to 'seek professional medical advice', in essence prompting interaction with the healthcare system and removing any potential accusations of practising medicine without a license.[38] Post-engagement confirmation testing and medical or pharmaceutical interventions however remain the exclusive purview of the medical sphere. With either company-initiated or consumer-initiated engagement, the *consumer* changes role to that of *patient*.

### *3.2.4 Flow-on effects of DTCGT*

Modelling of the industry space raised the question 'what would consumers do with the results.' The flow-on effects of consumers having DTCGT results or raw genetic data were considered with new modes of online peer-to-peer engagement identified. Options included voluntarily sharing genetic/health/medical/treatment details and receiving interpretation information and psychosocial support in online communities such as PatientsLikeMe.com and CureTogether.com. Those with raw data files could also use sites such as Promethease.com or Livewello.com to further interpret data for a larger range of health-related results, with both sites offering direct upload of files from major DTCGT companies.

Closer inspection revealed links between these sites and specific DTCGT companies such as corporate ownership of CureTogether.com by 23andMe and monetisation of resultant data such as PatientsLikeMe.com on-selling contributor data to pharmaceutical companies.[39] As consumer contributions increase in online communities, these sites, like DTCGT companies, will amass extremely valuable databases of both genotype and phenotype data. Further, it became standard

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[37] Ike Swetlitz, 'Genetic tests ordered by doctors race to market, while 'direct-to-consumer tests hinge on FDA approval' *Stat* 16 march 2019 <https://www.statnews.com/2018/03/16/genetic-tests-fda-regulations/>.

[38] See Amy McGuire and Wylie Burke, 'Health system implications of direct-to-consumer personal genome testing' (2011) 14 *Public Health Genomics* 53-58; Cynthia Marietta and Amy McGuire, 'Direct-to-consumer genetic testing: Is it the practice of medicine?' (2009) 37(2) *J Law Med Ethics* 369-374.

[39] See <http://news.patientslikeme.com/faq-item/faq/how-does-patientslikeme-make-money>.

practice for DTCGT companies to routinely and actively seek consumer agreement to conduct research on submitted samples and genetic results.

Figure 3.4 illustrates what consumers might do with their results and raw data files, including sharing with family, online communities, online interpretation sites, or with doctors or seeking additional disease-related information on DTCGT or general health websites. What is of note is that only engagement with healthcare professionals is within the medical sphere, all others remain firmly within commercial (online sharing) or personal spheres (sharing with family).

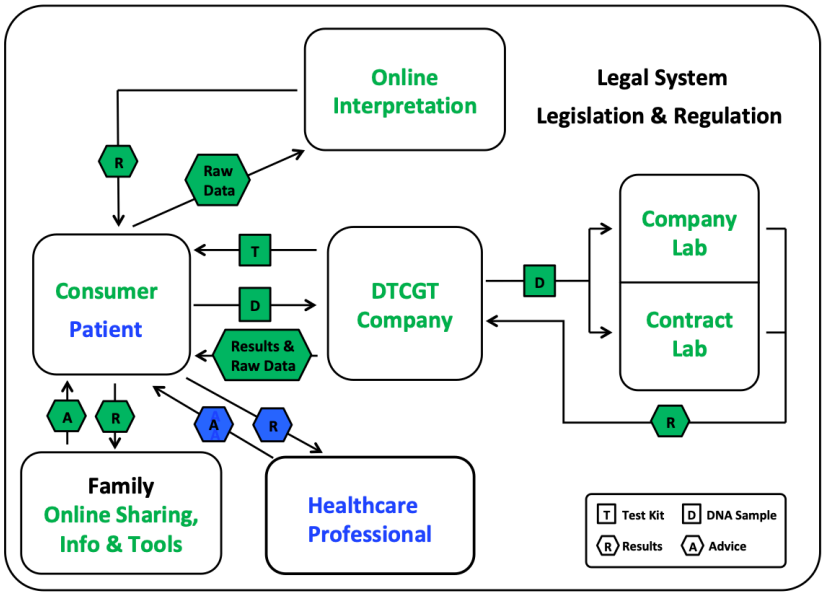


**Figure 3.4 DTCGT's flow-on effect**

### *3.2.5 Comparing DTCGT & CGT: The individual's perspective*

As illustrated in Figures 3.5 and 3.6, while the same basic stages are involved whether an individual chooses DTCGT or CGT, there are some notable differences. At any stage in the CGT process the individual can withdraw, while for DTCGT once samples are provided, results are returned – money paid, results delivered.

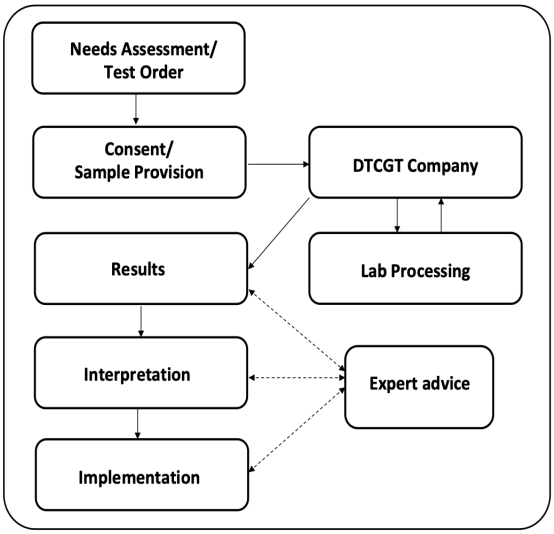


**Figure 3.5 DTCGT: Individual engagement**

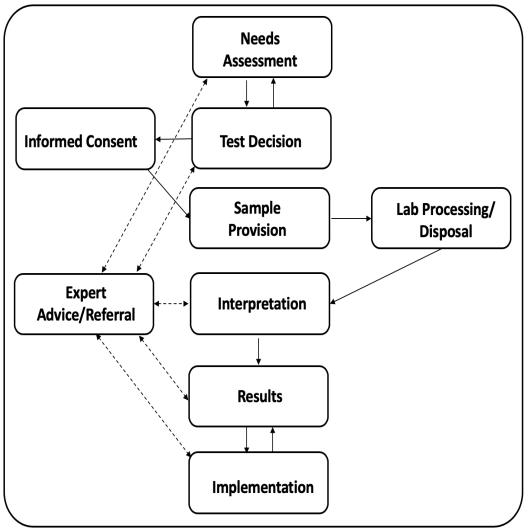


**Figure 3.6 CGT: Individual engagement**

### *3.2.5.1 Needs assessment*

With DTCGT, individuals conduct their own needs assessment determining purchase according to motivations previously discussed. However, for the DTCGT business model to be cost-effective and provide competitive value for consumers, the vast majority of companies offer bundled testing including a range of predictive, pharmacogenomic and carrier status tests (non-targeted testing).[40] As such, the individual decision is simply whether or not to order the bundle on offer, accepting whatever DTCGT tests their selected company offers.

Needs assessment for CGT is more complex as medical professionals must decide on the *specific* individual tests required to answer *specific* medical questions (targeted testing), consulting with patients at all stages. CGT decisions are evidence-based, taking into consideration symptoms, family history, medical or pharmaceutical history, lifestyle, patient concerns and readiness to deal with or action results. Specific tests are selected based on genes to be screened, mutations sought, availability to the specific patient according to testing criteria, and who would pay e.g. subsidisation and/or patient contribution, At this stage, pre-test genetic counselling is available if

[40] See Eline Bunnik, Maartje Schermer and Cecile Janssens, 'Personal genome testing: Test characteristics to clarify the discourse on ethical, legal and societal issues' (2011) *BMC Medical Ethics* DOI: 10.1186/1472-6939-12-11.

required.[41] While general guidance and information about CGT is provided to the profession, if needed, expert advice from genetics specialists can be sought.[42]

Doctors need a reason to test and any tests ordered must be clinically relevant. Generally, tests with no clinical utility are not ordered as prevention or treatment options are not available, however these may be ordered if judged necessary to alleviate extreme psychological distress. Communication during this process is two-way, with patients involved in all decisions.

#### *3.2.5.2 Consent, sample provision and lab processing*

*'Every human being of adult years and sound mind has the right to determine what shall be done with their own body'*[43]

Australia's healthcare system is built on the twin foundations of beneficence (moral imperative of doing right) and personal autonomy (the right of the individual to decide what *will* be done). The challenge in individual cases is to achieve balance between what may often be opposing rights. In cases of conflict where this delicate balance cannot be achieved, the right of competent individuals to either refuse or consent is generally upheld.[44] Obtaining informed consent after discussion of risks and benefits of medical tests including CGT and procedures is well established in health jurisprudence, both domestic and international, protecting individuals' right to make educated choices, even if that choice is contrary to medical opinion or potentially harmful.[45] In the absence of consent, the contact involved in providing healthcare services may expose the healthcare provider to criminal or tortious liability for assault or false imprisonment, for example.[46]

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[41] See Anon, 'Direct-to-Consumer genetic test results can be lost in translation' ePathWay, The Royal College of Pathologists of Australasia (2012) Issue 011, February, <http://epathways.rcpa.edu.au/one.html>.

[42] Australian Government, NHMRC, *Medical Genetic Testing Information for health professionals* (April 2010). <https://nhmrc.gov.au/about-us/publications/medical-genetic-testing-information-health-professionals>.

[43] *Schloendorff v Society of New York Hospital* 211 NY 125 (1914) Cardoza J at 126 - principle approved in *Australia in Secretary, Department of Health and Community Services v JWB and SMB* (Marion's Case) (1992) 175 CLR 218 at 310; international law e.g. UNESCO, *Universal Declaration on Bioethics and Human Rights* (2005), Article 6.

[44] Frank Stuart Kinsinger, 'Beneficence and the professional's moral imperative' (2009) 16 *Journal of Chiropractic Humanities* 44-46. For an illustration of an exception see *Mercy Hospitals Victoria v D1* [2018] VSC 519, where the court required a blood transfusion be given to a non-consenting Jehovah's Witness if necessary to save her life or prevent serious injury during upcoming induced labour.

[45] See *Rogers v Whitaker* (1992) 175 CLR 479 for discussion of whether all material information provided.

[46] For example, *Crimes Act 1900* (NSW) s61.

Consent is narrowly defined, with three elements required for validity: capacity to make treatment decisions; free and voluntary without undue pressure; and covering only the specific act performed.[47] Consent can be implied, verbal or in writing, with opportunities provided to seek clarification, expert advice or second opinions.[48]

Post-consent DNA sample collection is strictly controlled and conducted in sterile settings in either doctors' offices or laboratories, with careful verification of identity as outlined in the *Health Insurance Act 1973* (Cth) s16A(5AA). To be eligible for subsidisation, s16A(2b) of the Act requires use of accredited laboratories. Once testing is complete, samples are generally held for a short period of time before disposal in case retesting or further consented testing is required.[49]

Whether by mouse click or signature, DTCGT consumers consent when registering their sample for testing. This is done in the absence of expert advice relative to potential risks and consequences, including whether unwanted information would be provided.[50] It is at this stage contract formation occurs and consent requested for use of samples and data in research. DTCGT health-related tests pose particular challenges to the concept of 'informed' consent.[51] For example, given the difficulty of verifying identity either online or relative to samples, the potential exists for minors or others to be tested without their knowledge or consent.[52] Whether consent was provided freely, voluntarily and by those with capacity also cannot be verified, calling into question whether DTCGT consent can ever be 'informed'.[53] While provided with quality-controlled

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[47] Given by an adult (e.g. *Age of Majority Act 1974* (ACT)) with appropriate decision-making capacity for the specific health care (see *Chatterton v Gerson* [1981] 1 All ER 257). Generally, parents or legal guardians may give consent for those under age of majority (*Family Law Act 1975* (Cth) s61C). See *F v West Berkshire Health Authority* [1989] 2 All ER 545 regarding decision-making capacity; *Re T (Adult: Refusal of Treatment)* [1993] Fam 95 regarding undue influence; *Cadutti v ACT Health and Community Care* [2003] ACTSC 95 regarding specific act.

[48] See *Good Medical Practice: A Code of Conduct for Doctors in Australia* (2018) issued under s30 of the *Health Practitioner Regulation National Act 2009* (Cth). See also *Re T (Adult: Refusal of Treatment)* [1993] Fam 95 for discussion of exceptions to consent.

[49] See *Health Insurance Act 1973* (Cth) s16A.

[50] While 23andMe consent is online at sample registration and EasyDNA consent is paper sent back with sample, both obtain consent concurrent with sample provision.

[51] See Eline Bunnik, Cecile Janssens and Maartje Schermer, 'A tiered-layered-staged model of informed consent for personal genome testing' (2012) *European Journal of Human Genetics* 1-6; Katherine Wasson, 'Direct-to-consumer genomics and research ethics: Should a more robust informed consent process be included? (2009) 9 (6-7) *The American Journal of Bioethics* 56-58.

[52] See Heidi Howard, Denise Avard and Pascal Borry, 'Are the kids really alright? Direct-to-consumer genetic testing in children: are company policies clashing with professional norms?' (2011) 19 *European Journal of Human Genetics* 1122-1126. EasyDNA (www.easydna.com.au) tests for infidelity (hair/stain DNA analysis) and 23andMe's *DNARelatives* allow finding of unknown relatives, without their consent.

[53] Capacity to consent to healthcare is presumed until rebutted. See *Re MB* [1997] 2 FCR 514. See also Australian Law Reform Commission and Australian Health Ethics Committee in *Essentially Yours: The*

test kits, the environment within which samples are provided is unknown. As noted previously, laboratories may be either company-owned or contract, with the location and disposal of samples post-testing unclear.

#### *3.2.5.3 Results, interpretation, implementation and expert advice*

Perhaps one of the most significant differences is the order in which receiving and then interpreting results occurs in DTCGT and CGT and the flow-on to interpretation. With DTCGT, individuals receive their results in standardised template formats[54] and are then left to interpret what they mean for themselves. DTCGT results provide genetic information only; with companies stressing results do not constitute a diagnosis, avoiding any claims of unauthorised practice of medicine. Any additional disease information available on DTCGT websites tends to be general in nature and accessible only via by consumer choice.

Individual interpretation is personal and, while may be considered within the context of their health status, could also be 'gut' reaction with no context. Further, individuals are presented with all results of bundled tests so must interpret each result individually and then determine for themselves which ones are the more serious.[55] Based on interpretation and assessment of severity, individuals then decide what they are going to do based on their own determination of need. Expert advice can be sought by *choice* as individuals are under no obligation to disclose DTCGT results to anyone. Psychosocial support can be sought from family or in online communities, again if they choose to disclose. Communication during most of the DTCGT process is one-way: from company to consumer.

With CGT, results are returned to doctors who then interpret within the context of individuals' health status, with interpretation specific to each individual test ordered. Such interpretation is incorporated with other health information to generate a diagnosis then used to develop treatment and intervention plans if warranted. If required, doctors can seek expert advice prior to any patient communication. Individuals are presented with a 'package' – results, interpretation and implementation plans – with post-test counselling provided as required. Two-way communication ensures reasonable levels of understanding and comfort with test results and implementation plans, effectively mediating adverse effects or inappropriate behaviour. With

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*Protection of Human Genetic Information in Australia*, Report No 96 (2003) at 359. Recommended criminalisation of non-consensual genetic testing including DTCGT not actioned to date.

[54] Cost effectiveness dictates standardisation of results return.

[55] Some companies require individuals to confirm they wish to receive their results for particular tests such as Alzheimer's before they are provided.

CGT, an individual's doctor provides confirmation, contextualisation, counselling and comfort (psychosocial support). Further expert advice is assessed based on the *needs* of the individual.

As whole genome and exome sequencing becomes increasingly used in clinical settings, doctors will face the additional challenge of deciding whether all data provided needs to be interpreted or just that pertaining to the particular mutation at issue.

## PART THREE: PROTECTION FOR CGT *PATIENTS*

The medico-legal system within which CGT operates is extremely complex and the general protections afforded all patients, such as those offered under the Australian Charter of Healthcare Rights, are assumed adequate to protect CGT patients.[56] Regulatory theorists however have long recognised there is more to regulation than laws and other regulatory instruments.[57] Modelling of the CGT space identified high levels of professional and government oversight, with gatekeepers functioning as defacto regulators. Each gatekeeper provides specific protection for CGT patients.

Figure 3.7 illustrates three key categories of independent yet co-dependant gatekeepers: medical, financial and quality. Medical gatekeepers interact directly with patients while the other two groups operate behind the scenes. While the system may be a complex web with stringent and often duplicated regulation or oversight in some areas and gaps in others, at its core it seeks to protect CGT patients in their interactions with healthcare practitioners and ensures proper handling of sensitive genetic samples and resultant data. It aims to ensure all CGTs publicly subsidised are valid, and all laboratory results provided for use in patient management are accurate, consistent and adhere to accepted domestic and international standards. While in many ways CGT is simply another medical test, results have familial implications requiring medical gatekeepers to always consider ethical and social implications of testing.

[56] The Charter applies to all health settings and was endorsed by all Australian health ministers in 2008. Rights include, for example, the right to be informed about services, treatment options and costs. <https://www.safetyandquality.gov.au/wp-content/uploads/2012/01/Charter-PDf.pdf>.
[57] See John Braithwaite, *The Essence of Responsive Regulation* (2011) 44 UBC Law Review 475-520.

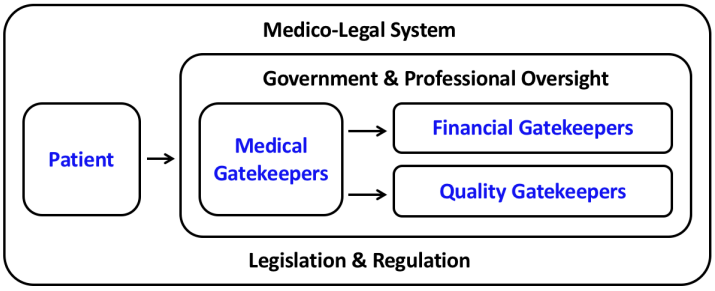


**Figure 3.7 Gatekeepers in CGT**

### *3.3.1 Medical gatekeepers: Doctors and genetic specialists*

From a patient perspective, the first gatekeepers encountered are medical gatekeepers. The *Health Insurance Act 1973* (Cth) only provides funding for eligible healthcare services (s10) rendered by registered healthcare practitioners (s3). As such, Australian patients can be assured medical gatekeepers are licensed by their respective professions, indicating they possess the applicable qualifications and experience necessary to determine if testing is clinically relevant, tests ordered have clinical utility, and advise provided relative to indicated medical and pharmaceutical interventions is sound. These medical gatekeepers also determine if counselling pre or post-testing is required. Access to genetic specialists is by general practitioner (GP) referral in most states and territories, although in certain instances individuals can self-refer for counselling. According to the NHMRC, 'the degree of counselling required depends on the level of uncertainty regarding the clinical implications of the test result, the potential implications for the patient, and the further implications for the patient's family.'[58]

As discussed previously, patients must give informed consent for CGTs and resulting medical, pharmaceutical or counselling intervention, with such testing and intervention occurring in situations where individuals are duty bound to keep information confidential.[59]

Access to test results and medical records is highly restricted. Australia's eHealth system provides a single online access point for secure and private sharing of patients' health information. However, participation is voluntary with patients themselves determining both information

[58] Australian Government National Health and Medical Research Council, *Medical Genetic Testing Information for Health Professionals* (April 2010), viii <https://www.nhmrc.gov.au/guidelines/publications/e99>.
[59] Legal duty of confidence is inherent in doctor-patient relationship. See *Coco v AN Clark (Engineers) Ltd* [1969] RPC 41, parties realise or should information is of confidential nature and should remain private.

available and registered providers allowed access.[60] For patients who opt-out, information is housed with individual providers, with consent required for sharing.

The designation 'patient' enlivens an established duty of care relationship in common law between patient and healthcare professional.[61] In *Rogers v Whitaker* (1992) 175 CLR 479, Mason CJ clearly stated: 'The law imposes on a medical practitioner a duty to exercise reasonable care and skill in the provision of professional advice and treatment.'[62] However, when a healthcare professional professes specialised skill or expertise such as genetics expertise, the standard is raised to that of a competent practitioner in the particular field of specialty.[63]

Medical negligence occurs when the standards deemed appropriate relative to the duty of care are breached and patient harm ensues.[64] At common law, such breaches occur when the healthcare practitioner has failed to take reasonable care, taking into consideration whether the risk was foreseeable, not insignificant, and whether a reasonable person would have taken precautions considering for example both the probability and seriousness of harm.[65] Historically, the *Bolam* test was used to determine if standards were breached, by considering whether a reasonable body of medical opinion supported the conduct.[66] However the *Bolam* test was rejected by the Australian High Court, concluding in *Rogers v Whitaker* (1992) that while 'evidence of acceptable medical practice is a useful guide', ultimate adjudication was the responsibility of the courts.[67]

In 2002, legislative reform of negligence law codified common law principles, with each state and territory enacting their own medical negligence laws, including type and quantum of remedies

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[60] See <http://www.ehealth.gov.au>.
[61] *Donoghue v Stevenson* [1932] AC 562 established general duty to take *reasonable* care to avoid *foreseeable* injury to a 'neighbour'. Civil liability laws such as *Civil Liability Act 2002* (NSW) s5O specifically address the standard of care expected of professionals.
[62] *Rogers v Whitaker* (1992) 175 CLR 479, at 5. See also, for example, *Civil Liability Act 2002* (NSW) s5O specifically addressing the standard of care expected of professionals
[63] See *Wilsher v Essex Area Health Authority* [1988] 1 All ER 87 (UKHL).
[64] Healthcare professionals owe a concurrent duty of care in tort and contract although most actions are based in tort. *AAA v BBB* [2005] WASC 139 and *Rosenberg v Percival* (2001) 205 CLR 434.
[65] See *Tame v New South Wales* (2002) 211 CLR 317 and *Gett v Tabet* [2009] NSWCA 76.
[66] See *Bolam v Friern Hospital Management Committee* [1957] 1 WLR 582, McNair J at 586 'a doctor is not guilty of negligence if he acted in accordance with a practice accepted as proper by a responsible body of medical men skilled in that particular art … merely because there is a body of opinion that would take a contrary view.' Also Lord Scarman's statement of the test in *Sidaway v Governors of Bethlem Royal Hospital* (1985) ACat 881.
[67] *Rogers v Whitaker* (1992) 175 CLR 479. In 2015, the UK also overruled *Bolam* in *Montgomery v Lanarkshire Health Board* [2015] UKSC 11 moving their position on information and advice nearer the AU position.

available and limitation periods.[68] Remedies available include compensatory and punitive damages for economic (e.g. lost wages) and non-economic (e.g. pain and suffering) loss as well as medical and ongoing care expenses.

CGT is also subject to a complex web of professional oversight of medical practitioners and genetic counsellors ensuring patients and their personal health information, in particular sensitive genetic data, are protected. Healthcare professionals require formal registration or licences to practice, with the Australian Health Practitioner Regulation Agency (AHPRA) providing the national registration and accreditation scheme and registry. The AHPRA is a statutory body under the *Health Practitioner Regulation National Law* (the National Law), in effect since 2010. While not Commonwealth legislation, each state and territories' legislative Acts contains the same National Law provisions: e.g. the objective 'to provide for the protection of the public by ensuring that only health practitioners who are suitably trained and qualified to practice in a competent and ethical manner are registered'.[69] It is an offence under the National Law punishable by fine to falsely use professional titles or claim registration of the 14 healthcare professions nationally regulated.[70]

The AHPRA operates in conjunction with the Medical Board of Australia (MBA), charged under the National Law with determining education requirements and ultimately registering medical practitioners.[71] The MBA, Australian Medical Association (AMA) and NHMRC are responsible for developing professional codes and guidelines for use in private practice and medical research.[72] As the MBA controls ongoing registration, it wields significant power over its members, ensuring compliance with all codes of practice and professional conduct e.g. seeking appropriate advice about disclosure of genetic information.[73]

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[68] Commonwealth of Australia, Ipp Committee, *Review of the Law of Negligence: Final Report*, September 2002; *Civil Liability Act 2003* (Qld). Despite aiming to achieve a uniform approach to personal injury claims this has not transpired.

[69] For example, see s3(2)(a) in the Schedule to the *Health Practitioner Regulation National Law (Victoria) Act 2009*.

[70] Division 10 Subsection 1 s113(1). Includes pharmacists, nurses and psychologists.

[71] See <http://www.medicalboard.gov.au/Registration-Standards.aspx>.

[72] See professional codes of ethics at <http://www.ama.com.au> and CGT guidance at NHMRC *Medical Genetic Testing Information for Health Professionals* (April 2010) <https://www.nhmrc.gov.au/guidelines/publications/e99>.

[73] Medical Board of Australia, *Good Medical Practice Code: A code of conduct for doctors in Australia* (March 2014) s3.4.4.

The Human Genetics Society of Australasia (HGSA) certifies genetic counsellors, again developing specific codes, guidelines and educational requirements.[74] Patients with complaints or concerns both pre and post CGT have recourse through the AHPRA and MBA complaint procedures or through state and territory Ombudsmen.[75]

### *3.3.2 Quality and financial gatekeepers: What's on offer and who pays?*

Medicare is illustrative of an organisation performing a dual role as both quality and financial gatekeepers. Medicare functions as a quality gatekeeper determining CGTs to be subsidised and a financial gatekeeper determining levels of subsidisation. For CGTs to be subsidised they must be on the MBS, which only occurs after evidence-based analysis to determine analytic validity, clinical validity and clinical utility.[76]

Analytically valid tests measure the presence or absence of specific gene variants e.g. BRCA1 tests must measure mutations on chromosome 17, position 21.[77] Clinical validity involves determining whether the mutation is related to the presence, absence or risk of a particular disease and varies by test.[78] Tests for monogenic diseases have high clinical validity as definitive diagnoses are provided, while those for polygenic or multifactorial conditions have lower clinical validity, as they are predictive, indicating susceptibility.[79]

Tests with clinical utility provide prevention, diagnosis or treatment information of use in healthcare decision-making.[80] Tests providing such information for individuals, families and healthcare professionals are judged to have high clinical utility, while those not providing such

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[74] See HGCA 'Guidelines for Training and Certification in Genetic Counselling' <http://www.hgsa.org.au/documents/item/1593>.
[75] The National Law establishes a National Health Practitioner Privacy Commissioner and the Office of the National Health Practitioner Ombudsman <http://www.nhpopc.gov.au>; States also provide services e.g. Health Complaints Commissioner for Tasmania <http://www.healthcomplaints.tas.gov.au>.
[76] See Wylie Burke, 'Genetic Tests: Clinical Validity and Clinical Utility' (2014) 81(9) *Curr Protoc Hum Genet* DOI: 10.1002/0471142905.hg0915s81; ACCE model developed by US Centre for Disease Control and Prevention's Office of Public Health Genomics <http://www.cdc.gov/genomics/gttesting/ACCE/>; Genetics Home Reference, 'How can consumers be sure a genetic test is valid and useful?" <https://ghr.nlm.nih.gov/primer/testing/validtest>.
[77] Genetics Home Reference <http://ghr.nlm.nih.gov/handbook/testing/validtest>; <http///ghr.nlm.hih.gov/gene/BRCA1>.
[78] Genetics Home Reference <http://ghr.nlm.nih.gov/handbook/testing/validtest>.
[79] See Royal College of Pathologists of Australasia, 'What should I know about direct-to-consumer genetic testing?' <https://www.rcpa.edu.au/getattachment/c7768ade-842d-4c9d-852a-6e38656964f8/FctSht-9-DrctConsumerGenTesting.aspx>.
[80] Genetics Home Reference <http:// http://ghr.nlm.nih.gov/handbook/testing/validtest>.

information have traditionally been judged to have low, if any, clinical utility.[81] In a narrow sense, tests for conditions with no known treatment or cure such as Alzheimer's disease have low clinical validity, however they may have personal utility.[82] For example, counselling interventions may improve physical and mental life quality and test results assist in financial decision-making, representing relevant metrics, even in the absence of traditional clinical benefits.

Figure 3.8 outlines the organisations involved in deciding which CGTs are listed on the MBS and therefore eligible for subsidisation for *all* Australians regardless of location. A similar system is in place for pharmaceuticals, which must be on the PBS to attract subsidisation and must be dispensed by registered pharmacists.[83]

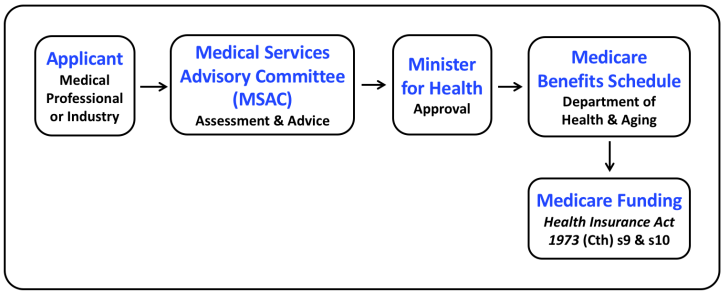


**Figure 3.8 How CGT gets on the MBS**

The process for obtaining Medicare approval is time-consuming and often contentious given escalating costs, budgetary constraints and patient/practitioner demand. In 2009, the Commonwealth government established the Medical Services Advisory Committee (MSAC) as the sole source of expert appraisal for its evidence-based framework for managing the MBS. The MSAC advises the Minister of Health as to comparative safety, benefits (e.g. clinical utility) and cost effectiveness of CGTs based on available evidence. If approved, CGTs are added to the MBS,

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[81] See Morris Foster, John Mulvihill and Richard Sharp, 'Evaluating the utility of personal genomic information' (2009) 11(8) *Genetics in Medicine* 570–574; David Hunter, Muin Khoury and Jeffrey Drazen, 'Letting the Genome out of the Bottle – Will We Get Our Wish?' (2008) 358(2) *The New England Journal of Medicine* 105-107.

[82] See Mauro Turrini and Barbara Prainsack, 'Beyond clinical utility: The multiple values of DTCGT genetics' (2016) 8 *Applied & Translational Genomics* 4–8; Eline Bunnik, Cecile Janssens and Maartje Schermer, 'Personal utility in genomic testing: is there such a thing?' (2014) *J Med Ethics* DOI: 10.1136/medethics-2013-101887; Ilona Kopits, Clara Chen, Scott Roberts, Wendy Uhlmann and Robert Green, 'Willingness to pay for genetic testing for Alzheimer's disease: A measure of personal utility' (2011) 15(12) *Genetic Testing and Molecular Biomarkers* 871-875.

[83] The PBS Advisory Committee of experts advises the Commonwealth Department of Human Services of therapeutic benefits and cost-effectiveness compared to alternative therapies (<www.pbs.gov.au/pbs/home>).

making them eligible for subsidisation.[84] The MBS and PBS also control access and funding for medical, pharmaceutical or counselling interventions required post-testing.

Medicare also sets the schedule fee for each approved CGT, conditions under which it will be funded such as symptoms or pathology and mandatory requirements. For example, counselling is required before testing for Fragile X syndrome affecting intellectual abilities. Medicare provides 75-85% subsidisation for CGT laboratory fees as well as general practitioner and specialist charges.

In reality, the MBS subsidises comparatively few CGTs; most are subsidised by state and territory governments from their Commonwealth-allocated health budgets for *selected* patients from their respective jurisdictions.[85] Testing is conducted through specialised clinics in each State's public health system, generally on referral from GPs, with criteria for access varying by state. To illustrate this complexity of the dual responsibilities for healthcare and its potential inequities across Australia, consider the case of previous state/territory subsidisation for BRCA 1/2 testing. Even though eligibility was based on risk, specific criteria varied by jurisdiction. As such, it was possible for one patient to obtain fully subsidised testing, while their genetic relative in another jurisdiction would have to bear the full cost. In late 2017, after substantial debate and lobbying, subsidised access to CGT was granted to *all* women diagnosed with breast cancer considered at high genetic risk under the MBS.[86]

Ability to access non-subsidised CGT depends on individual financial capacity, as private health insurance only covers CGT for patients already admitted to hospital.[87] For example, those wanting cystic fibrosis carrier testing must bear the full cost. According to Cystic Fibrosis Australia, most parents of CF children did not know their carrier status indicating low incidence of screening, although whether due to low awareness or test cost is unknown.[88]

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[84] *Health Insurance Act 1973* (Cth) s9 and s10. See <www.mbsonline.gov.au> Group 7 Genetics.
[85] For a discussion of the complexity of state and federal funding of CGTs, see Dianne Nicol, Jane Nielsen and Verity Dawkins, 'The genetic diagnostic testing industry in Australia' in Centre for Law & Genetics *D'Arcy v Myriad Genetics* (2018) Occasional Paper No 9, Chapter 4. See overview of CGT and counselling services on a state and territory basis at <http://www.genetics.edu.au/Genetics-Services>.
[86] See Anon, 'BCNA welcomes new Medicare rebates for genetic testing' (2017) *BCNA News* 12 October <https://www.bcna.org.au/news/2017/10/bcna-welcomes-new-medicare-rebates-for-genetic-testing/>. MBS Item73295 sets the schedule fee at $1200 with subsidisation between $800 and 1160. <www9.health.gov.au/mbs>.
[87] Personal communication with three of Australia's main private health insurers.
[88] See <http://www.cysticfibrosis.org.au/vic/carrier-screening>.

### 3.3.2.1 Quality gatekeepers: Ensuring CGT and testing quality

Two quality gatekeepers are of note: the Therapeutic Goods Administration (TGA) ensuring CGT quality and the National Association of Testing Authorities (NATA) accrediting laboratories.

#### *The Therapeutic Goods Administration*

The *Therapeutic Goods Act 1989* (Cth), as administered by the TGA, governs the safety, quality and performance of therapeutic goods either supplied within Australia or imported and exported. The TGA applies scientific and clinical expertise to ensure benefits to individuals outweigh any risks associated with use. Therapeutic goods are defined as those 'represented in any way to be, or that are … likely to be taken to be for therapeutic use'.[89]

Therapeutic use is defined as use in or in connection with (a) preventing, diagnosing, curing or alleviating a disease, ailment, defect or injury (*disease diagnosis*); (b) influencing, inhibiting or modifying a physiological process (*pharmacogenomics*); (c) testing the susceptibility of persons to a disease or ailment (*disease susceptibility*); and (d) influencing, controlling or preventing conception (*carrier status*).[90] While these definitions are quite broad, covering everything from tongue depressors to medicines and programmable pacemakers, they also clearly capture a range of CGTs (as noted in parentheses).

The *Therapeutic Goods (Medical Devices) Regulations 2002* (Cth), effective July 2014, provides the regulatory framework for 'in vitro medical devices' defined as 'any instrument, apparatus, appliance, material or other article …used alone or in combination …' for 'diagnosis, prevention, monitoring, treatment or alleviation of disease' or 'control of conception' amongst others.[91] This is the *only* Australian legislation specifically capturing manufacture and supply of CGTs.

Amendments to these regulations passed in 2010 had already established a regulatory regime specifically for in-vitro diagnostic devices (IVDs), as a subset of medical devices.[92] IVDs are pathology tests and related instrumentation such as reagents and specimen receptacles used to test human samples for clinical diagnosis or management.[93] IVDs must be intended by manufacturers to be used *in* vitro for examination of specimens originating in the human body

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[89] *Therapeutic Goods Act 1989* (Cth), s3 definition of therapeutic goods.
[90] Ibid s3 definition of *therapeutic use* a, b, c and d.
[91] Ibid Division 2 s41BD definition of *medical device* (i) and (iv).
[92] *In vitro* refers to testing conducted outside an organism's body *cf. in vivo* conducted inside the body.
[93] *Therapeutic Goods (Medical Devices) Regulations* 2002 (Cth) Dictionary 161 for full definition of *IVD medical device*.

solely or principally for the purpose of providing information about a physiological or pathological state, a congenital abnormality or to monitor therapeutic measures.

Prior to 2010, regulation of IVDs was limited, with the vast majority exempt from any form of pre-market scrutiny, with the notable exceptions of HIV and Hepatitis C tests given their public health implications. The amendment clearly captures CGTs ensuring regulatory scrutiny prior to supply and ongoing monitoring. IVDs are classified according a four-tier risk based system based on the risk posed to health from incorrect results (false positives or false negatives) with Class 1 representing the lowest and Class 4 the highest risk to individual or public health, such as infectious diseases.[94] The level of initial assessment and ongoing monitoring varies with risk classification.[95] CGTs are deemed to be Class 3 indicating moderate public health and high personal health risk where incorrect results could lead to significant detriment relative to patient management decisions, including the potential for patient distress.[96]

It is the responsibility of manufacturers of both over-the-counter and laboratory-based tests to ensure proper classification and adherence to specific requirements for their class of IVDs.[97] All therapeutic goods including CGTs must be registered on the Australian Register of Therapeutic Goods (ARTG)[98] as a condition of legal supply and must also comply with the Essential principles and Conformity assessment procedures as required by the Act.[99] The Essential principles are designed to ensure safety and performance with the Conformity assessment procedures ensuring quality assurance and post-market monitoring including reporting of adverse events.[100] Non-

[94] Ibid Schedule 2A for classification rules for IVD medical devices.
[95] The TGA is a member of the International Medical Devices Regulators Forum, a voluntary association of regulators whose aim is to facilitate international medical device regulatory harmonisation and convergence. See <http://www.imdrf.org> for full details.
[96] See NHMRC, *DNA Genetic Testing in the Australian Context: A Statement from the National Medical Health Research Council* (2012) <https://www.nhmrc.gov.au/about-us/publications/dna-genetic-testing-australian-context>. See also Australian Government, Department of Health, Therapeutic Goods Administration, 'IVD medical devices: Definitions & links' <https://www.tga.gov.au/ivd-medical-devices-definitions-links>.
[97] *Therapeutic Goods Act 1989* (Cth) Chapter 4 Division 2 s41BG. For flowcharts outlining classification rules, see Australian Government, Department of Health, Therapeutic Goods Administration, *Guidance for IVD sponsors – A roadmap to market* (2011) <https://www.tga.gov.au/guidance-ivd-sponsors-roadmap-market>; 'Classification of IVD medical devices' Version 2.0 December 2015, 5.
[98] See *Therapeutic Goods Act 1989* (Cth) Chapter 4 Part 4-5 for registration details.
[99] Ibid Chapter 4, Division 1 s41BA. Additional information as well as the searchable Register <http://www.tga.gov.au/industry/artg.htm#.VB4ciksWFFw>.
[100] Ibid Chapter 4 Division 2 s41BH and s41BI. See also Chapter 4, Part 4-2 for detail on Essential principles and Chapter 4, Part 4-3 for detail on Conformity assessment standards.

compliance with any provision of the *Therapeutic Goods Act 1989* (Cth) attracts penalties ranging from fines to imprisonment.[101]

### *The National Association of Testing Authorities (NATA)*

To ensure analytic and clinical validity, Medicare and state/territory subsidisation is only provided for CGTs deemed necessary by treating practitioners and conducted by approved pathologists at accredited laboratories.[102] Prior to 2014, laboratory accreditation was not mandatory, prompting the NHMRC to note 'accreditation of medical genetic laboratories is currently dictated by the funding mechanism rather than a commitment to accurate test results'.[103]

NATA is recognised as the national authority for laboratory accreditation for all Medicare and state/territorial CGTs.[104] Figure 3.9 outlines the NATA accreditation process.

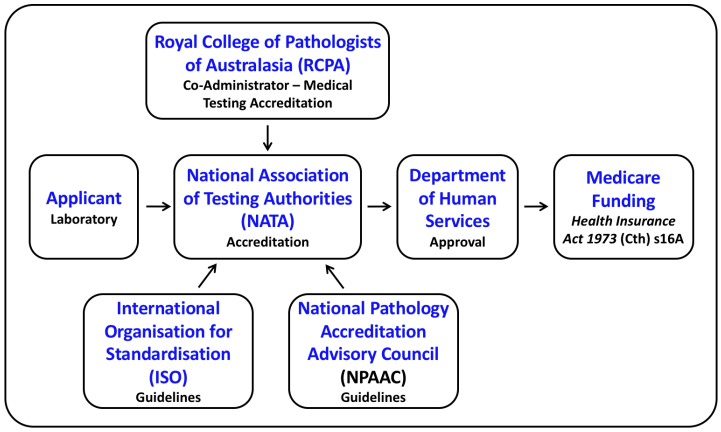


**Figure 3.9 NATA accreditation**

NATA and the Royal College of Pathologists of Australasia co-administer the accreditation process with NATA conducting all accreditation assessments and audits for medical testing laboratories, recommending approval to the Department of Health. Accredited laboratories conducting subsidised CGTs must comply with international standards, in particular ISO 15189, which outlines

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[101] Ibid Chapter 4 Division 1 s41JB (3) where fines are imposed for individuals failing to comply with s41JA notices and (4) where imprisonment for 5 years and/or fines for individuals providing false or misleading information in response to s41JA notices where use of the medical device has, would or would likely cause harm or injury.

[102] *Health Insurance Act 1973* (Cth): deemed necessary s16A(1a); approved pathology practitioner at approved laboratory s16A (2b) (a) and (b).

[103] Australian Government, NHMRC *Medical Genetic Testing Information for Health Professionals* (April 2010), 25 <https://www.nhmrc.gov.au/guidelines/publications/e99>.

[104] See Memorandum of Understanding <http://www.nata.com.au/nata/phocadownload/publications/government/MoU-Cwlth-NATA.pdf>.

quality control measure for sample collection, analysis and training.[105] The National Pathology Accreditation Advisory Council develops and maintains standards required under The *Health Insurance (Accredited Pathology Laboratories – Approval) Principles 2002* for pathology accreditation.[106] NPAAC has also developed specific minimum standards for laboratories conducting human nucleic acid testing such as independent processing of duplicate samples for predictive CGTs.[107]

### 3.3.3 A complex web of protection … but can it keep pace with genetic discoveries?

This overview has identified *some* of the gatekeepers charged with keeping Australia's CGT patients safe. Protection is provided by a complex labyrinth of rules, regulations, policies and procedures influenced by intergovernmental agreements, international conventions and agreements, as well as professional oversight - all relying on the input of 'experts' in each field who it can be assumed find current levels of protection adequate. Gatekeepers and regulators, in attempting to keep up with advances in the field of genetics, however have tended to 'graft on' new provisions to existing legislation and regulation rather than creating *sui generis* legislation, or have taken a 'wait and see' adverse outcomes approach.[108]

As CGTs become 'increasingly integrated into healthcare', the rate of genetic discoveries accelerates and general awareness of testing benefits develops, Commonwealth, state and territorial governments will undoubtedly come under patient and practitioner pressure to offer more CGTs.[109] However, the complexity involved in offering more CGTs has significant time and cost implications, potentially resulting in *protracted* translation of genetic discoveries into genetic testing, clinical applications and patient management.

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[105] See <http:www.iso.org>.
[106] See NATA, 'Medical testing field application document: Requirements for accreditation' November 2013 for interpretation of NPAAC and ISO requirements <www.nata.com.au>.
[107] See Australian Government Department of Health, NPACC *Requirements for Medical Testing of Human Nucleic Acids* (2013) NPAAC <http://www.health.gov.au/internet/main/publishing.nsf/Content/health-npaac-docs-nad2.htm>.
[108] See TGA explanation and procedures for reporting adverse incidents by both individuals and medical professionals <https://www.tga.gov.au/reporting-adverse-events> and <https://www.tga.gov.au/publication/reporting-medical-device-adverse-incidents>.
[109] The Royal College of Pathologists of Australasia, 'New nationwide research on genetic testing in Australia' Media release, 22 February 2019 <https://www.rcpa.edu.au/News-and-Media-Releases/Media-Releases/Docs/New-nationwide-research-on-genetic-testing-in-Aust>.

# PART FOUR: PROTECTIONS FOR DTCGT *CONSUMERS*

As noted previously, the potential exists for the CGT and DTCGT spheres to merge when there is consumer or company-initiated engagement with healthcare. In both of these instances, once DTCGT *consumers* enter their doctors' surgeries, they enter as *patients*, afforded all of the protections discussed in Part Three. Even with the standard DTCGT e-commerce model (Figure 3.1), there is overlap between the protections afforded in both medical and commercial spheres. The commercial nature of DTCGT means it naturally falls within the ambit of consumer protection legislation. The definition of consumer has broadly been held to include what are often referred to as 'health consumers' (an increasingly popular term used for patients). For example, in *E v Australian Red Cross Society* (1991) 27 FCR 310, a hospital patient receiving nursing care was deemed a consumer. However, the nature of what DTCGTs offer also brings it within the regulatory ambit of the TGA. Other heads of law that might provide protection to Australia's DTCGT consumers such as general contract are beyond the scope of this research.

## *3.4.1 The role of the TGA*

DTCGTs for disease diagnosis, disease susceptibility, pharmacogenomics and carrier status are clearly captured by the therapeutic use definition but also fall into the self-testing IVD medical devices definition (key aspects italicised).[110] Self-testing IVDs are defined as those intended to be used:

> '(a) in the home or similar environment by a lay person; or
>
> (b) in the collection of a sample by a lay person and, if that sample is tested by another person, the results are returned directly to the person from whom the sample was taken without the direct supervision of a health professional who has formal training in the medical field or discipline to which the self-testing relates.'[111]

Home glucose meters commonly used by diabetics, for example, would fall within section (a) and are classified as Class 1, while DTCGTs offered via the standard e-commerce model fall within section (b). While most IVDs for self-testing are classified as Class 3, there are exceptions if they are not used for determining a 'serious condition, ailment or defect' such as pregnancy testing or where testing is preliminary.[112] Whether DTCGT disclaimers that results are provided for

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[110] *Therapeutic Goods Act* (Cth) 1989, s3 definition of *therapeutic use* a, b, c and d.
[111] *Therapeutic Goods (Medical Devices) Regulations 2002* (Cth) Dictionary, 161.
[112] Ibid Schedule 2A s1.4(a) and (b).

'research, information and education only' and are not a diagnosis would qualify them to claim testing is preliminary is doubtful, as many of the tests are for clearly serious conditions.

The *Therapeutic Goods (Excluded Purposes) Specifications 2010* (Cth), in force since July 2010, provides direction as specifically what constitutes excluded purposes under the Act[113] and applies specifically to self-testing IVDs.[114] Self-testing IVDs are excluded if their purpose is to 'determine the presence of, or predict susceptibility to, diseases in humans', 'diagnose, aid in diagnosis or indicate the presence of a serious disease or condition...' and 'test for the presence of markers that are precursors to a serious disease or condition...' amongst others.[115] Serious disease is defined a disease that (a) may result in death or long-term disability; and (b) may be incurable or require major therapeutic interventions; and (c) must be diagnosed accurately, to mitigate the public health impact of the disease.'[116] Manufacturers seeking to register self-testing IVDs on the ARTG making them legal for sale in Australia must certify they are not intended for any of the excluded purposes.[117]

While this would appear to specifically make it illegal to sell DTCGTs in Australia, there are points of ambiguity.[118] Self-testing IVDs do not fall within s41BE of the Act if 'the device is *also* to be used for another purpose'[119] *including* Commonwealth or state/territory public health screening, 'for self-testing to monitor a diagnosed disease or condition', or for export only.[120] Given the bundled nature of DTCGT testing, many companies include trait and ancestry in addition to health-related testing which might arguably exempt them from Excluded Purposes prohibitions. DNA tests for paternity, ancestry, traits and sporting ability do not fall within the TGA's definition of 'therapeutic use'. What is also unclear is specifically what would be covered – sample receptacles, tests, results, or interpretation. It is also not an offence to purchase DTCGTs not listed on the ARTG 'for use in the treatment of the importer, or a member of importer's immediate family, or for use in the in vitro examination of a specimen obtained from the importer or a member of the

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[113] *Therapeutic Goods Act 1989* (Cth) Chapter 4 Division 2 s41BEA Excluded purposes.
[114] *Therapeutic Goods (Excluded Purposes) Act 2010* (Cth) 4(1).
[115] Ibid 4(2)(b)(c) and (d). Cancer and myocardial infarction are mentioned specifically as to diagnosis exclusion and Pap smear and Prostate cancer tests for presence of markers exclusion.
[116] *Therapeutic Goods (Medical Devices) Regulations 2002* (Cth) Dictionary, 175.
[117] *Therapeutic Act 1989* (Cth) Chapter 4 Division 1 s41FD(ia) and 41FF(1A). s41BEA provides for specification, by legislative instrument, of excluded purposes.
[118] Dianne Nicol and Meredith Hagger, 'Direct-to-consumer genetic testing – a regulatory nightmare?' (2013) 198(9) *Medical Journal of Australia* 501-502.
[119] *Therapeutic Goods (Excluded Purposes) Act 2010* (Cth) 4 s2.
[120] Ibid 4 s3.

importer's immediate family' and those for non-commercial export.[121] This means not only can Australians purchase from DTCGT companies offering bundled tests both onshore and offshore (personal use exemption) but such tests are exempt from the quality, safety and monitoring provisions required of CGTs. As an example of the former, consider EasyDNA, a DTCGT company whose Terms and Conditions state its jurisdiction as Australia, and whose products have been integrated into prominent Australian television shows.[122] EasyDNA offers a range of tests including ancestry in addition to genetic predisposition tests. Given the range of tests that could be provided from analysis of the same sample, the company would likely be outside the TGA's authority, although the 'also for another purpose' provision would have to be tested by the TGA, the company or the courts, none of which has happened to date.

### *3.4.2 The role of Australian consumer protection law*

The United Nations Guidelines for Consumer Protection set out the main characteristics for effective consumer protection legislation, including provision of consumer safety, promotion of economic interests, access to adequate information, enhanced consumer awareness and competencies, effective redress mechanisms, consumer participation in political decision-making, and promotion of sustainable consumption patterns.[123] These are what Australia's consumer protection laws and enforcement seek to provide.

From 2011, *all* Australian consumers are provided with the *same* protections and *all* businesses are under the *same* obligations under the *Australian Consumer Law* (ACL), contained in Schedule 2 of the *Competition and Consumer Act 2010* (Cth).[124] The ACL draws on the Productivity Council's 2008 *Review of Australia's Consumer Policy Framework* and replaces all existing national and state consumer laws,[125] an important step towards ensuring consistency of protection for all Australians.

The ACL seeks to 'improve consumer wellbeing through consumer empowerment and protection, fostering effective competition and enabling the confident participation of consumers in markets in which both consumers and suppliers trade fairly.'[126] The law reflects a combination of three

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[121] *Therapeutic Goods (Medical Devices) Regulations 2002* (Cth) Schedule 4 part 1 (1.1) and (1.2).
[122] Terms and Conditions Item 10 <www.easydna.com.au>. See also 'As featured on' section of homepage.
[123] United Nations Conference on Trade and Development, *United Nations Guidelines for Consumer Protection* (2016), United Nations <https://unctad.org/en/PublicationsLibrary/ditccplpmisc2016d1_en.pdf>.
[124] Replacing the Trade Practices Act 1974 (Cth).
[125] For example, *Fair Trading Act 1989* (Qld); *Door to Door Trading Act 1986* (Tas); *Lay by Sales Agreements Act 1963* (ACT).
[126] *Intergovernmental Agreement for the Australian Consumer Law* 2 July 2009, Recital C.

general prohibitions and rule-based regulation prohibiting specific types of conduct.[127] General prohibitions against misleading and deceptive conduct, unconscionable conduct, and unfair contract terms provide Australian consumers with a basic 'safety-net' of minimum standards and businesses with the basic norms of conduct expected in Australia's marketplace. The ACLs general prohibitions were developed using a principles-based approach, allowing for flexible application without seeking to provide exhaustive lists. Being broad provisions, these general provisions lack clarity and certainly, thus requiring judicial interpretation. Rules-based regulation prohibiting specific behaviours such as pyramid selling provide certainty and clarity; however also provide unscrupulous businesses with opportunities to operate outside tightly defined prohibitions.

While the ACL does not specifically address genetics, its provisions *could* apply to DTCGT. However, whether they *would* apply would depend on ACCC enforcement action and/or judicial interpretation. Although discussing the application of all ACL provisions to DTCGT is beyond the scope of this research, the general provisions prohibiting misleading or deceptive conduct (s18) and unfair contract terms (s23) have general application so would apply to the DTCGT offering. Section 18 prohibits a person in trade or commerce from engaging in conduct that is misleading or deceptive or is likely to mislead or deceive and could apply to the full range of DTCGT activities, particularly their marketing messages.[128] Misleading or deceptive conduct is determined using an objective test, which, when making representations to the public considers ordinary or reasonable members of the class of prospective buyers.[129] Intention to mislead or deceive is not a necessary element, with the courts looking at the effect of actions. DTCGT marketing messages will be discussed further in Chapter Four (4.1.3).

Section 23 prohibits unfair contract terms with such terms considered void in standard form contracts although the remainder of these contracts bind if the unfair terms can be severed.[130] 'Unfair' terms cause significant imbalances in parties' rights and obligations, are not reasonably necessary to protect legitimate interests of advantaged parties, and could cause detriment (financial or otherwise) if applied or relied upon.[131] Courts must take into account whether the

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[127] See Jeannie Marie Paterson and Gerard Brody, 'Safety net consumer protection: Using prohibitions on unfair and unconscionable conduct to respond to predatory business models' (2015) 38 *Journal of Consumer Policy* 332-355.

[128] *Australian Consumer Law* Schedule 2, Chapter 2, Part 2-1, s18(1). Trade or commerce includes 'within Australia and between Australia and places outside Australia and includes any business or professional activity (whether or not carried on for profit). Schedule 2, Chapter 1 Section 2 Definitions.

[129] See *Campomar Soiedad Limitada v Nike International Ltd* (2000) 202 CLR.

[130] *Australian Consumer Law* Schedule 2, Chapter 2, Part 2-3 s23(1) & (2). A consumer contract is one for supply of goods or services to an individual for personal, domestic or household use or consumption.

[131] Ibid Chapter 2, Part 2-3 s24(1) a, b & c. A non-exhaustive list of examples is provided in s25.

term is transparent and the contract as a whole, although may consider other matters considered relevant.[132] DTCGT contracts by their nature fall within the s27 definition of standard form contracts as companies have all or most of the bargaining power, prepare contracts before discussions relating to specific transactions, consumers can either accept or reject but not negotiate terms, and terms do not take into account specific characteristics of the other party or the transaction.[133] DTCGT contract terms will be discussed further in Chapter Four (4.1.2).

DTCGT offerings may also be captured under various specific protections. For example, s29 prohibits the making of false or misleading representations about goods or services such as meeting particular standards or qualities, or the need to acquire them and would most certainly capture DTCGT marketing messages. Sections 33 and 34 cover misleading conduct concerning the suitability for purpose and quality of any goods or services, again covering marketing messages but possibly also results.[134] Australian consumers are also provided with a range of guarantees that function as the minimum standard expected of companies such as goods being of *acceptable* quality and fit for purpose, and are not excludable by contract.[135] For example, should sample receptacles and genetic tests not be captured by the TGA, s29 *may* apply. Although given corporate viability relies on receiving safe, uncontaminated samples, the receptacles are likely 'fit for purpose', as are any tests that rely on peer-reviewed science.

### *3.4.3 Enforcing the ACL: The role of the ACCC*

The Australian Competition and Consumer Commission (ACCC) and each of the state and territory consumer law agencies are responsible for enforcement of the ACL.[136] The ACCC is an independent Commonwealth statutory authority charged with enforcing all aspects of the *Competition and Consumer Act 2010* (Cth), promoting competition, fair trading and regulating national infrastructure. The ACCC is *selective* in the matters investigated and sectors where their own market analysis and education programs is undertaken, focusing on those with the greatest potential to harm the competitive process or result in widespread consumer or small business detriment. It rarely becomes involved in individual consumer-initiated complaints, leaving that to state and territory agencies or industry-specific regulators.

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[132] Ibid Part 2-3 s24(2) a & b. 'Transparent' is defined in s24(3) a through d and includes 'expressed in reasonably plain language'. S24(4) places the burden on advantaged parties to prove terms 'reasonably necessary'.
[133] Ibid Chapter 2, Part 2-3 s27(1) & (2).
[134] Ibid Chapter 3, Part 3-1 s29(1)a, b and l, s33 and s34.
[135] Ibid Chapter 3, Part 3-2 s54(2)a. s64 ensures no provisions contained in Division 1 – Consumer Guarantees may be excluded by contract.
[136] For example, Queensland Office of Fair Trading and Consumer Affairs Victoria.

The ACCC's efforts are guided by its enduring priorities as well as those set annually. One of its ensuring priorities is the protection of vulnerable and disadvantaged consumers. Disadvantaged consumers have ongoing attributes or circumstances such as poor education while vulnerability may occur because of personal characteristics or context such as purchasing at times of emotional stress or where quality is difficult to ascertain. Given the DTCGT offering with its high credence qualities discussed earlier and the emotive nature of DTCGT results, it is arguable all DTCGT consumers are vulnerable to a certain degree. Interestingly, one of the ACCC's 2019 priorities is the impact of collection and use of consumer data by digital platforms, with a focus on transparency and adequacy of disclosure.[137] This may well call attention to DTCGTs company use of consumer data and that of genetic data voluntarily shared in online communities.

The ACCC uses a range of tools to ensure compliance, such as consumer education and enforces the non-compliance provisions in the ACL. Chapters Four and Five of the ACL provide a range of offences and remedies including monetary penalties, administrative resolutions, infringement notices, court-enforceable undertakings, and criminal proceedings. The ACL also outlines available defences, such as reasonable mistake of fact (s207). When deciding which compliance and enforcement tool to use, the ACCC's first priority is achieving the best outcome for the community while managing risk, ensuring its responses are proportionate to conduct and resulting or potential harm. The ACCC operates transparently, publicising all enforcement activities and, while independent, is ultimately accountable to Parliament and the courts.

Unlike the TGA, whose jurisdiction is limited to Australia, the ACL has extraterritorial effect given inclusion of 'between Australia and places outside Australia' in its definition of 'trade and commerce',[138] and the ACCC's international agreements with several overseas regulators.[139] Even though Australia has legislation concerning enforcement of foreign judgements, the lack of consistent rules for determining jurisdiction suggest it may not be straightforward to enforce Australian protections for online DTCGT activities.[140]

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[137] ACCC, *2019 ACCC Enforcement and Compliance Priorities* <https://www.accc.gov.au/system/files/2019%20Enforcement-and-Compliance-Priorities.pdf>.
[138] *Australian Consumer Law* Schedule 2, Schedule 2, Chapter 1 Section 2 Definitions.
[139] ACCC, *Treaties and Agreements* (2013) <https://www.accc.gov.au/about-us/international-relations/treaties-agreements>.
[140] See Australia's *Foreign Judgments Act 1991* (Cth). See *Dow Jones & Company Inc v Gutnick* (2002) 194 ALR 433 (place of damage = place of publication), *Calder v Jones* 465 US 783 (1984) (effects plus website targeting) and *Zippo Manufacturing v Zippo.com* 952 F Supp 1119 (WD Pa 1997) (sliding scale of interactivity).

### 3.4.5 Enforcing consumer protections: DTCGT in the sights of regulators and in the Courts

While the necessary first step, regulation requires effective enforcement and if need be, interpretation in the courts.

#### 3.4.5.1 The Australian experience

There had not been a lot of enforcement activity in Australia's DTCGT space, but what there has been shows a willingness to address DTCGT claims and enforce the ACL. In January 2011, Western Australia's Consumer Protection Commissioner issued a warning about unsolicited DNA test kits appearing across Australia. The kits, mailed from China, used the name of a legitimate but unconnected Canadian company. The enclosed letter asked consumers to provide credit card details for processing fees and personal information to enter a prize draw. In exchange, the company promised 'DNA model may be configured, even positioned and programmed, for stunning success, physical and mental health, affluence, significant accomplishment and the deepest sense of personal fulfilment – empowering you with a built-in edge to prosper and excel in ways you never dreamed possible.' The service was deemed 'worthless and dubious' and an international scam.[141]

In September 2016, the ACCC accepted an administrative undertaking from pharmacy chain Chemmart regarding 'representations regarding the effectiveness of a myDNA genetic test in identifying an individual's response to certain drugs'. The test, supplied by myDNA Life Australia Pty Ltd, sold for $A149 and was not covered by Medicare, state and territory subsidisation or private insurance. The ACCC expressed concern that promotional efforts (e.g. infomercials, in-store brochures) conveyed a 'false or misleading impression' regarding the test's usefulness and appropriateness to particular consumers, noting genetic factors are only one factor used to determine specific drugs and dosages. Further they noted the high level of trust placed in pharmacists and the expectation information provided would be clear, accurate and explain both benefits and limitations. In response, Chemmart withdrew all promotional materials and agreed to refrain from making future statements that might mislead consumers.[142]

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[141] Katherine Fenech, 'DNA test scam warning' *WA today* 5 January 2011 <https://www.watoday.com.au/national/western-australia/dna-test-scam-warning-20110105-19fjz.html>.
[142] ACCC, EBOS Group Ltd, on behalf of its subsidiary Symbion Pty Ltd, the owner of the Chemmart pharmacy franchise, MR 166/16 <https://www.accc.gov.au/media-release/chemmart-agrees-to-improve-its-promotion-of-%E2%80%9Cmydna%E2%80%9D-tests>.

While the TGA has not been active in the DTCGT space, in November 2018 the first HIV self-test was registered on the ARGT, making it legal for sale after the ban on supply lifted in 2014.[143] HIV tests are Class 4 IVDs (high public and personal health risks due to infectious nature) with self-tests deemed presumptive requiring confirmation of positive results via diagnostic lab tests.[144] The TGA acknowledged HIV self-tests were available online from offshore providers but these had not been evaluated by the TGA for safety and performance.[145] Whether a similar approach might apply to DTCGTs ultimately leading to their inclusion on the ARGT remains to be seen.

### *3.4.5.2 The US experience*

United States regulators have been more active with the Food and Drug Administration (FDA), Federal Trade Commission (FTC) and the Courts all taking aim at DTCGT. Given the similarities in regulatory structures (Figure 3.10) their activities provide insight and guidance to their Australian counterparts.

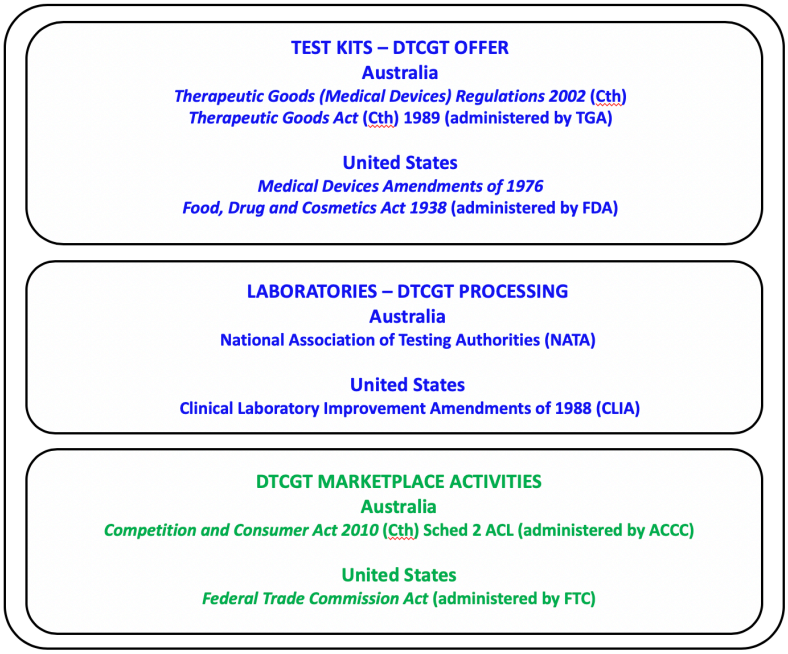


**Figure 3.10 AU & US DTCGT regulatory structure.**

In the US, medical devices, including IVDs, come under the regulatory authority of the *Food, Drug and Cosmetics Act 21 U.S.C. 321 1938* (FD&C) as amended by the *Medical Devices Amendments of*

[143] Atomo Diagnostics Pty Ltd., Atomo HIV self-test, ARGT ID 311989 <http://search.tga.gov.au/s/search.html?collection=tga-artg&profile=record&meta_i=311989>.
[144] Australian Government, Department of Health, Therapeutic Goods Administration, 'Classification of IVD medical devices' Version 2.0 December 2015, 19.
[145] Australian Government, Department of Health, Therapeutic Goods Administration, 'HIV testing in Australia' 5 December 2018 <https://www.tga.gov.au/hiv-testing-australia>.

*1976*, with enforcement administered by the FDA, similar to Australia's *Therapeutic Goods Act (1989)* and the TGA. Medical devices are defined as an 'instrument … implant … in vitro reagent … etc.' intended for '… use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment or prevention of disease … to affect the structure or function of the body'.[146] The FDA also uses risk-based classification, assigning devices into three classes: Class I low risk, exempt from pre-market review; Class II moderate risk requiring premarket notification; and Class III high risk requiring premarket approval.[147] The FDA also has authority to perform post-market reviews and monitors adverse incidents.

Laboratories performing health-related genetic testing are subject to federal standards for proficiency, quality and personnel expertise under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) administered by the Centers for Medicare & Medicaid Services (CMS).[148] The CLIA and FDA complement each other with CLIA assessing analytic validity and clinical validity, similar to Australia's NATA and TGA. Individuals, healthcare professionals and insurance providers determine clinical utility. However, not all DTCGT providers use CLIA labs and just as many DTCGTs offer non-FDA approved DTCGTs. Those that offer FDA approved DTCGTs and use CLIA labs typically promote both of these facts as significant selling features.[149] DTCGT companies' marketplace activities come under the regulatory ambit of the *Federal Trade Commission Act* of 1914 as administered by the FTC,[150] similar to Australia's ACL and ACCC.

### *FDA activities: Let the regulatory dance begin*

In 2010 the FDA began issuing 'it has come to our attention' letters to a number of companies exercising its pre-market assessment authority over DTCGT tests, which it believed fell within the meaning of s201(h).[151] This 'shot over the bow' caused some industry angst. It also generated commentary such as that referring to classifying tests as medical devices 'quite a stretch, legally',

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[146] Food, Drug and Cosmetics Act 21 U.S.C. 321 s201(h)1 & 2. Comparable to definitions in the *Therapeutic Goods Act* (Cth) and *Therapeutic Goods (Medical Devices) Regulations 2002*.

[147] Food, Drug and Cosmetics Act 21 U.S.C. 321, Chapter 5, Part A Sec. 510 (outlines requirements) & Sec. 513 (outlines classes).

[148] Comparable to NATA accreditation. Research labs testing human samples but not reporting patient specific results for diagnosis etc are exempt from CLIA standards. States can opt out of CLIA, enforcing their own standards.

[149] See Giuseppe Lippi, Emmanuel Favaloro and Mario Plebani, 'Direct-to-consumer testing: more risks than opportunities' (2011) 65(12) *International Journal of Clinical Practice* 1221 – 1229.

[150] Comparable to ACL and ACCC.

[151] Letters sent to Pathway Genomics, 23andMe, deCode Genetics and Navigenics amongst others. See FDA correspondence <https://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/ucm111104.htm>.

with some companies reverting back to physician ordered processes.[152] What is of interest however is that no company overtly challenged the FDA's determination, or sought clarification as to what specifically was covered, tacitly accepting the FDA's authority.

Although 23andMe began the FDA process, it failed to provide the required assurances tests were analytically and clinically valid, despite repeated requests. At the end of 2013, the FDA sent 23andMe a very strongly worded, at least in bureaucratic terms, 'warning letter' stating concerns over potential consumer outcomes such as reliance on pharmacogenomic tests to self-manage prescriptions but most importantly ordered the company to 'immediately discontinue marketing' until FDA market authorisation was obtained.[153] The company complied, stopping offering its 254 health-related tests, focusing its efforts on ancestry and trait testing, while providing all its customers with raw data files.[154]

However, its 'regulatory dance' with the FDA continued with the company complying with FDA procedures to obtain the FDA's first DTCGT approval to market its Bloom syndrome carrier screening test in 2015. At the time, the FDA also 'downclassified' all carrier tests to Class II thereby exempting these tests from premarket review. The FDA combined the criteria used for over-the-counter drugs that average consumers understand how and when to use, with the clinical validity required of genetic tests, providing a regulatory framework for future submissions.[155]

In 2017, 23andMe obtained approval for ten disease predisposition tests including Parkinson's, late-onset Alzheimer's and Celiac disease. Excluded however were genetic tests that function as diagnostic tests, often the sole basis for significant treatment decisions. Reliance was placed on peer-reviewed scientific literature establishing genetic links, and corporate studies showing clinical accuracy, a departure from requiring clinical trials. The FDA evaluated a 23andMe

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[152] See Andrew Smith, 'Cautious evolution underway in DTC genetic testing' 12 February 2016 *OncLive* <https://www.onclive.com/publications/oncology-live/2016/vol-17-no-4/cautious-evolution-underway-in-dtc-genetic-testing>. Quoting Jennifer Wagner.

[153] FDA letter to 23andMe, 22 November 2013, <https://www.fda.gov/iceci/enforcementactions/warningletters/2013/ucm376296.htm>.

[154] These files, of course could be uploaded into online interpretation sites generating health-related results.

[155] Aaron Krol, 'What Comes Next for Direct-to-Consumer Genetics?', 16 July 2015 <www.bio-itworld.com>. Quoting Hank Greely and Elizabeth Mansfield of the FDA.

corporate-derived user study demonstrating consumers understood test instructions finding reports easy to understand.[156]

In 2018, the FDA permitted the company to market, with special controls, certain pharmacogenomic tests, again complying with scientific and consumer evidence requirements.[157] Also authorised was the company's BRCA test, a test specifically noted in the FDA's 2013 warning letter due to concern inaccurate results might prompt needless mastectomies.[158]

In 2017, the FDA also acknowledged DTCGT doesn't fit within its traditional risk-based approach, indicating the need for a streamlined, more flexible regulatory approach. With this approach the FDA will now conduct a one-time review to ensure the company is meeting FDA requirements, after which the company can enter the market with new tests without further review. Special controls can also be required including requirements for assessing 'accuracy, reliability and clinical relevance' and the studies and data required to demonstrate performance.[159] Whether the one-time review and special controls if required provide adequate protection for consumers remains to be seen.[160]

Comparison of early 'come to our attention' letters, 23andMe's 'cease and desist' 2013 directive, and recent FDA statements reflects a softening stance, with the FDA committed to encouraging DTCGT development and creating less burdensome pathways that are 'risk-based, efficient, achieve the assurance of safety and efficacy…', while acknowledging 'genetic risk testing can provide helpful information about an individual's predisposition for certain diseases and

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[156] FDA news release, 'FDA allows marketing of first direct-to-consumer tests that provide genetic risk information for certain conditions' 6 April 2017 <https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm551185.htm>.
[157] FDA news release, 'FDA authorises first direct-to-consumer test for detecting genetic variants that may be associated with medication metabolism' 31 October 2018 <https://www.fda.gov/NewsEventsNewsroom/PressAnnouncements/ucm624753>.
[158] Sarah Zhang, '23andMe will now test for BRCA breast-cancer genes' *The Atlantic* 6 March 2018 <https://www.theatlantic.com/health/archive/2018/03/23andme-brca-breast-cancer/554957>.
[159] FDA Statement, 'Statement from FDA Commissioner Scott Gottlieb, M.D., on implementation of agency's streamlined development and review pathway for consumer tests that evaluate genetic health risks' 6 November 2017 <https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm583885.htm>.
[160] For in-depth analysis of the FDA processes, see Margaret Curnutte, 'Regulatory controls for direct-to-consumer genetic tests: a case study on how the FDA exercised its authority' (2017) 36(3) *New Genetics and Society* 209-226.

conditions …' and 'can prompt consumers to be more engaged in pursuing … healthy lifestyle choices … and more aware of their health risks.'[161]

In 2012, then commissioner Margaret Hamburg, noting the FDA can only enforce laws passed by Congress, commented that 'One of the challenges is the world has been evolving and yet we have legislation that reflects a different era.'[162] The softening stance of the FDA in its interpretation of those laws may be reflective of the regulatory – or more precisely anti-regulatory – priorities of the current US government or may be reflective of a growing acknowledgement of the benefits of validated DTCGTs.[163] In either case, the take-away for Australian regulators is that rigid regulatory structures can change – or at least flex – when regulators are motivated.

### *The FTC: Actively policing misleading and deceptive genetic claims*

The FTC has broad authority to protect consumers from unfair and deceptive trade practices such as false and misleading advertising under Section 5(a) of the FTC Act 15 U.S.C. 45(a)(1) coupled with investigative and enforcement authority. In 2014, the FDA issued final consent orders against GeneLink, Inc. and its former subsidiary foru™ International Corp in its first enforcement action against 'marketers of purported personalized genomics products'.[164] These companies marketed nutritional supplements claimed to treat diseases such as diabetes and heart diseases customised to each consumers' DNA assessment to 'compensate for genetic disadvantages'. What is notable in this case is the FTC's baseline requirement that genetic claims be 'true and supported by at least two adequate and well-controlled studies', reinforcing the need for claims to be based on 'competent and reliable scientific evidence'.[165]

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[161] FDA Statement, 'Statement from FDA Commissioner Scott Gottlieb, M.D., on implementation of agency's streamlined development and review pathway for consumer tests that evaluate genetic health risks' 6 November 2017 <https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm583885.htm>.

[162] David Kroll, 'Why the FDA can't be flexible with 23andMe, by law' 28 November 2013 *Forbes* <https://www.forbes.com/sites/davidkroll/2013/11/28/why-the-fda-cant-be-flexible-with-23andme-by-law/#174fa8a43fc1>. Quoting Margaret Hamburg.

[163] Each commissioner leaves their mark so Commissioner Gottlieb's unexpected resignation in early 2019 may result in more changes once a permanent replacement is named.

[164] A respondent can elect to pursue consent orders, neither admitting nor denying allegations but waiving rights to judicial review. The companies were also found to have inadequately protected consumers' personal information. Final consent order <https://www.ftc.gov/system/files/documents/cases/140512genelinkdo_0.pdf>.

[165] See FTC news releases, 'Companies pitching genetically customized nutritional supplements will drop misleading disease claims' 7 January 2014 <https://www.ftc.gov/news-events/press-releases/2014/01/companies-pitching-genetically-customized-nutritional-supplements>; 'FTC approves final consent orders settling charges that companies deceptively claimed their genetically modified nutritional supplements could treat disease', 12 May 2014 <https://www.ftc.gov/news-events/press-releases/2014/05/ftc-approves-final-consent-orders-settling-charges-companies>.

In 2010, L'Oréal USA, Inc. also agreed to final consent orders concerning unsubstantiated claims its Génifique and Youth Code facial creams boosted genetic activity and targeted users' genes providing anti-aging benefits.[166] While not DTCGT, the FTC still required scientific evidence but did not provide specifics, suggesting DTCGTs would be held to a higher evidentiary standard.

### *DTCGT in the Courts*

Shortly after the FDA's 2013 'cease and desist' letter to 23andMe, multiple actions were filed alleging false and misleading advertising based on misrepresentations about the health benefits of the company's Personal Genome Service (PGS) and unfair business practices. The first class action, *Casey v 23andMe Inc. et al.*, filed in the US District Court for the Southern District of California, made extensive references to the FDA's warning letter, alleging breach of implied warranties and unjust enrichment amongst others, seeking restitution for costs, punitive damages and injunctive relief to prevent continued advertising.[167] In 2014, the claims were consolidated as a class action in the Northern District of California under the name *Tompkins v 23andMe, Inc*., alleging the PGS had no analytical or clinical validity. [168] 23andMe filed an omnibus motion to compel arbitration as per its Terms of Service. What followed were a series of motions and countermotions, with the clause eventually upheld in 2016 in the Court of Appeals for the Ninth Circuit and a proposed settlement agreed.[169] The class was defined as US consumers who purchased the PGS for personal use between 16 October 2007 and 22 November 2013. Eligible class members who submitted claims could elect for either $US40 coupon towards 23andMe test kits or $US12.50 compensation. Class members who did not submit a claim by 6 December 2017 received coupons.[170] While civil suits can be an effective way to shape industry practices as they deal with actual rather than speculative harm, in this instance no ruling on the factual allegations was made so neither confirmation nor denial of the clinical validity of DTCGT was established, with resolution solely based on terms of the contractual agreement.[171]

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**166** FTC news release, 'L'Oréal settles FTC charges alleging deceptive advertising for anti-aging cosmetics', 30 June 2014 <https://www.ftc.gov/news-events/press-releases/2014/06/loreal-settles-ftc-charges-alleging-deceptive-advertising-anti>.

167 Case No. 3:13-cv-02847-H-JMA filed in the federal court for the Southern District of California, 27 November 2013.

168 Case No. 5:13-CV-05682-LHK.

169 *Tompkins v 23and Me, Inc.,* 840 F.3d 1016 (2016). Arbitration known as Karen Davis-Hudson and Sarah Diaz v 23andMe, Inc, AAA Case No. 74-200-1400-0032.

170 Full details <http://www.23andmesettlement.com/faqs.aspx>.

171 Jennifer Wagner 'Troubles keep coming for 23andMe' 5 December 2013 posting <www.genomicslawreport.com>.

## PART FIVE: DTCGT RESEARCH: THANKS FOR THE SPIT!

Individuals wishing to contribute to medical or genetic research have traditionally participated in clinical trials, contributed samples to medical researchers for specific projects, or deposited samples in biobanks where governance procedures determine researcher access. Much of this research is funded either directly or indirectly by public expenditure, with the expectation public safety and basic rights of participants are respected, and results will ultimately inform general healthcare. Guidance for the former comes from the 1964 Declaration of Helsinki developed by the World Medical Association and the 1997 UNESCO Declaration on the Human Genome and Human Rights.[172] The Declaration of Helsinki sets out the basic pillars of human research practice providing a set of ethical principles such as obtaining informed consent. Protection of individual research subjects is the priority above medical research's primary purpose of generating new knowledge. The UNESCO declaration specifies 'research, treatment and diagnosis affecting an individual's genome shall be undertaken only after rigorous and prior assessment of the potential risks and benefits' with informed consent and prior review of research protocols.[173]

Medical research in Australia must comply with guidelines contained in the *National Statement on Ethical Conduct in Human Research* (2007), reflecting principles from both Declarations including informed consent and review by independent ethics committees.[174] Research *on* humans (medical research) is held to higher ethical standards with extensive justification of need for research required, than research *with* humans (social sciences research).

With the emergence of DTCGT, individuals now have an additional pathway – consenting for their genetic samples and test results to be used by the same companies they paid to provide their genetic results. Whether samples and results are used in company research, on-sold to other companies such as pharmaceuticals for their research, or data access provided to academic and medical researchers, the individual can now assume an additional role to the previously discussed *patient* and *consumer* – that of *research participant* (Figure 3.11).

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[172] Full declaration <https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/>.
[173] Articles 5, 10, 11 and 12 *Declaration of Human Genome and Human Rights*, General Conference of UNESCO, 29th session, 11 November 1997.
[174] Full statement made in accordance with the *National Health and Medical Research Council Act 1992* <https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018>. Further information on Australian domestic health research guidelines can be found in Chapter 20, Ben White, Fiona McDonald and Lindy Willmott, *Health Law in Australia 3e* (Lawbook Co., 2018).

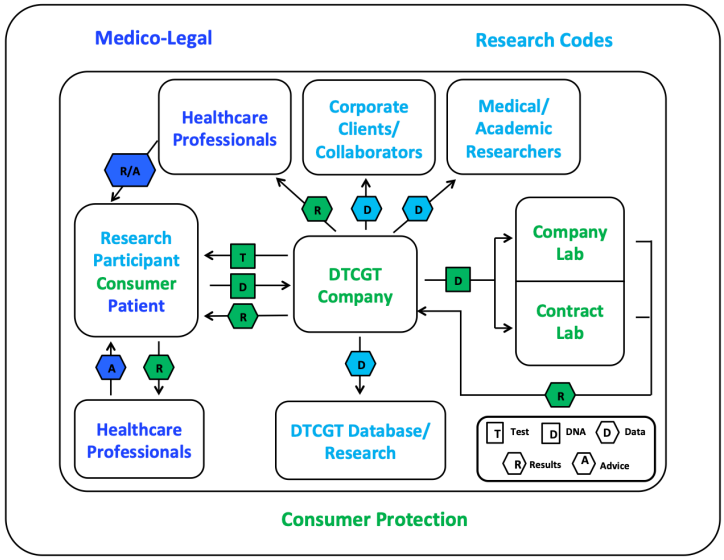


**Figure 3.11 Adding a new role for individuals – research participant**

While the history of medical research is by no means unblemished,[175] adding DTCGTs interested in 'research for profit' into the mix raises a raft of concerns in particular surrounding informed consent and ethical standards. These concerns are discussed throughout Chapter Four (e.g. 4.1.2.1 Genetic privacy).

## PART SIX: DO WE NEED SPECIFIC CONSUMER PROTECTION REGULATION TO PROTECT DTCGT CONSUMERS?

As noted in Chapter One (1.2), this research applies both a legal and consumer behaviour lens to DTCGT, making for a natural focus on consumer protection. The ACL is designed to protect *all* consumers in *all* marketplace activities whether what is purchased is a chocolate bar, haircut or insurance policy, with mandatory consumer guarantees assumed to provide adequate baseline protection.[176] Consumers themselves are assumed able to judge if there is an issue e.g. electrical appliance won't turn on, item ordered as blue arrives as red. And it is consumers themselves who are required to initiate complaints and remedy procedures. Standard remedies under these guarantees of 'replace, repair or refund' are relatively straightforward to calculate, and deemed

[175] See the Nuremberg Code 1947 developed post World War II in response to 'medical research' atrocities detailed in the Nuremberg trials. The Code contains ten requirements for permissible medical experimentation, the first of which is voluntary consent. <https://history.nih.gov/research/downloads/nuremberg.pdf>.

[176] While businesses cannot opt-out of these consumer guarantees, they are free to supplement e.g. 'change of mind' return policies.

adequate to return consumers to their original state as expected in torts e.g. a $5 refund for an item costing $5.[177]

However, the core question remains as to whether the protections afforded Australians under the ACL are sufficient if the purchase is a DTCGT for breast cancer or Alzheimer's – or is there a need for consumer protection specific to DTCGT? DTCGT operates outside the traditional healthcare protections afforded CGT patients. As individuals must self-interpret, DTCGT also has the potential for negative consumer outcomes, especially so if DTCGT results are used to make significant treatment, prevention and lifestyle decisions.[178] Additionally, the legal duty to take reasonable care to avoid causing emotional distress is well established in tort, with accidental infliction, if negligent, sufficient to support a cause of action in the courts.[179] Emotional distress, however, is much more difficult for consumers to determine and is a lot less straightforward to both quantify and determine remedies by regulators.

### *3.6.1 The Consumer Policy Toolkit: Guiding Australian consumer policy and enforcement*

When evaluating consumer protection policy and deciding on enforcement targets, Australia's regulators and the ACCC utilise the *Consumer Policy Toolkit* (CPT) developed by the Organisation for Economic Cooperation and Development (OECD).

In 2010, an OECD working party including the Australian Treasury developed the CPT focusing on end consumers, acknowledging the impact of changing market and consumer landscapes such as technological advances, market liberalisation and expanded choice of goods and services available both on and off-shore. It also draws on our increased understanding of the nature of consumer decision-making. Classical economic theory has always assumed consumers make rational well-informed marketplace decisions designed to satisfy their needs and wants, so the focus should be on insuring consumers are provided with full and honest information.[180] Insight from fields such

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[177] For example, in tort the purpose of compensatory damages is to place the plaintiff as far as possible in the position they would have been had the wrong not occurred. See *Livingstone v Rawyards Coal Co* (1880) 5 App Cas 25.

[178] See Nick Bansback, Sonia Sizto, Daphne Guh and Aslam Anis, 'The Effect of Direct-to-consumer Genetic Tests on Anticipated Affect and Health Seeking Behaviors: A Pilot Survey' (2012) 16 *Genetic Testing and Molecular Biomarkers* 1165-1171.

[179] The tort action is for wilful infliction of nervous shock but requires proof of actual damage such as psychiatric illness and is available under limited circumstances – *Wilkinson v Downton* [1897] 2 QB 57.

[180] Ivo Vlaev, 'Logical choices: Rationality and the contextuality of decision-making' (2018) 8(1) *Brain Science* DOI: 10.3390/brainsci8010008.

as consumer behaviour and behavioural economics suggest in reality consumers often do not behave rationally, making decisions with limited information for a range of motivations.[181]

The CPT was developed as a 'practical guide that is designed to aid policy makers in using a systematic approach to identify and evaluate consumer problems and to develop, implement and review effective consumer policies so that consumers can play their role in ensuring a dynamic economy.'[182]

The CPT has been adopted by Australian regulators with additional guidance provided by *Consumer policy in Australia: A companion to the OECD Consumer Policy Toolkit* (2011) developed specifically to 'provide practical information and advice to government officials and those interested in consumer policy when considering consumer policy issues in an Australian context'.[183]

The CPT suggests the primary focus should be the potential for consumer detriment when assessing whether policy reform or enforcement is warranted. The ACCC has acknowledged the focus of its enforcement activities is to minimise actual or potential consumer detriment.[184] As consumer detriment is the key driver of both policy and enforcement, regulators need evidence-based data as to the potential for detriment inherent in the DTCGT offering which this research seeks to provide.

#### *3.6.1.1 The CPT's six-step approach to policy development*

The CPT suggests a six-step approach to consumer policy development, with the following non-prescriptive steps providing guidance. At the end of the following six steps, regulators should be in a position to decide whether to continue, modify or terminate specific consumer protection policies (Figure 3.12).

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[181] Jan Charbonneau, Michael Solomon, Greg Marshall and Elnora Stuart, *Marketing: Real People, Real Choices* 2e (Pearson New Zealand, 2011), Chapter 4 Consumer and Organisational Behaviour.
[182] OECD, *Consumer Policy Toolkit* (2010) OECD Publishing, DOI: 10.1787/9789264079663-en, 9.
[183] Commonwealth of Australia, *Consumer policy in Australia: A companion to the OECD Consumer Policy Toolkit* (2011) iv <http://consumerlaw.gov.au/files/2015/09/Companion_to_OECD_Toolkit.pdf>.
[184] *Compliance and enforcement: How regulators enforce the Australian Consumer Law* (Commonwealth of Australia 2010); <https://www.accc.gov.au/about-us/australian-competition-consumer-commission/compliance-enforcement-policy>.

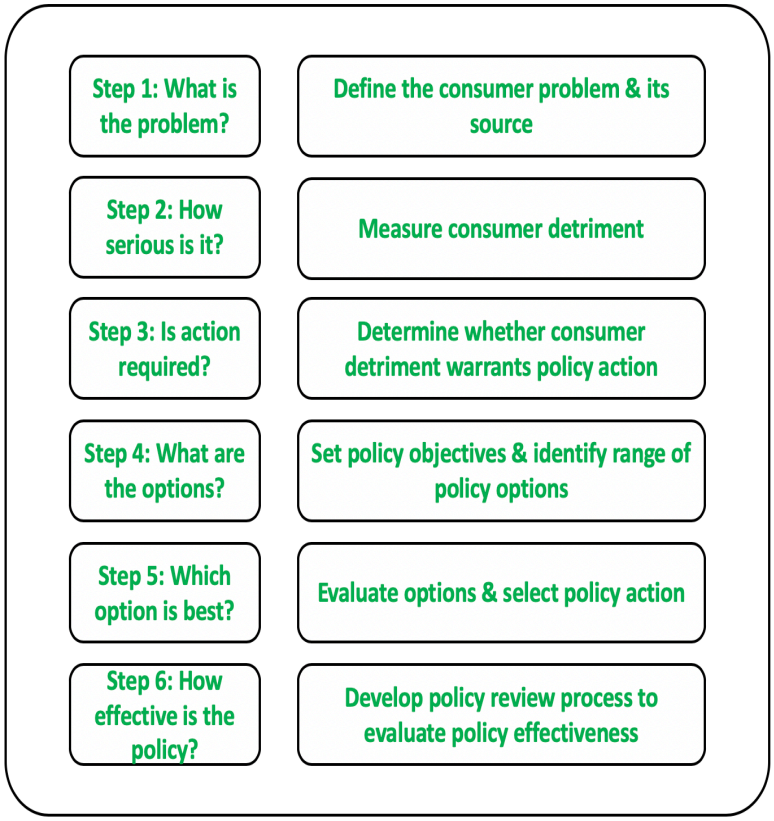


**Figure 3.12 Six step policy development**[185]

This research focuses specifically on Steps 1 and 2 of the CPT as problem definition and quantifying the potential for consumer detriment are the necessary first steps before legislators can determine whether policy action is warranted. Simply, if there is no consumer detriment or that found is judged not sufficient, there is no need for consumer protection.

### *Step 1: Defining the problem*

> *'The unprecedented speed with which high-throughput techniques for extracting genetic information are being translated into commercial products – bypassing traditional professional and regulatory gatekeepers – has left scientists and clinicians playing catch-up.'*[186]

Also playing catch-up are regulators and enforcement agencies.

Step 1 of the CPT requires problem identification. At its core, the overarching problem is DTCGT's commercial nature. Unlike the time and resource intensive processes outlined in Part Three to protect CGT patients, one of DTCGT companies' key strengths is its ability to move quickly, driven by the commercial imperative of profitability. However, while the CGT processes have the

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[185] OECD, *Consumer Policy Toolkit* (2010) OECD Publishing, DOI: 10.1787/9789264079663-en, 11.
[186] Bridget Kuehn, 'Risks and Benefits of Direct-to-Consumer Genetic Testing Remain Unclear' (2008) 300(13) *JAMA* 1503, 1503.

potential for *protracted translation* of genetic discoveries into accessible genetic testing and flow-on treatment, DTCGT has the potential for *premature translation*. 'As soon as someone publishes a paper with an association, someone can start testing the next day', meaning time from lab to market may be faster than the rigours of the science can be tested and replicated.[187] DTCGT companies have also structured their operations to limit their responsibility well beyond disclaimers and contract terms. The genetic associations and markers used in developing tests derive from the peer-reviewed science of the day, placing responsibility for analytic and clinical validity on scientists. In many instances, although DTCGT companies make use of the same genome-wide association studies (GWAS) and scientific evidence as CGT providers, they move on their results much faster. Provided accredited laboratories are used, these labs bear responsibility for clinical validity. In terms of interpretation and resulting actions, this is left to individuals or the medical profession if individuals choose to share. As such individuals and/or their doctors bear responsibility for determining clinical utility.

### *Step 2: Measuring consumer detriment*

Consumer detriment broadly refers to the loss in consumer welfare incurred when market outcomes fall short of their potential.[188] Consumer detriment is an outcome, although its causes are not always apparent. Enhanced understanding of its causes however is essential for determining appropriate policy responses, as different forms require different policy responses. When determining whether policy action is required, regulators are encouraged to consider the scale of consumer detriment, who is experiencing it (e.g. vulnerable groups) and anticipated duration. Action may be warranted if the detriment is large but experienced by a small group of consumers or the detriment is small but experienced by a large group of consumers.[189]

The CPT divides consumer detriment into two broad categories – structural and personal, providing a non-exhaustive list of situation-dependent examples for guidance. While there is no universally accepted definition of consumer detriment, these CPT categorisations are reflective of two extensive literature reviews conducted in 2006 for the UK office of Fair Trading and in 2007 by Europe Economics.[190]

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[187] Bridget Kuehn, 'Risks and benefits of direct-to-consumer genetic testing remain unclear' (2008) 300(13) *Journal of the American Medical* Association, 1503-1505, 1503. Quoting Lawrence Brody then of the National Human Genome Research Institute.
[188] OECD, *Consumer Policy Toolkit* (2010) OECD Publishing, DOI: 10.1787/9789264079663-en, 52-55.
[189] Ibid 12.
[190] Peter Lund, Laura Miller, Johanna Körting and Joseph Ungemah, *The psychology of consumer detriment: A conceptual review* (2006) Office of Fair Trading OFT792.

*Structural detriment* arises from market conditions that limit consumer choices and/or inflate prices and generally affects consumers in the *aggregate*. Structural detriment, representing a loss of consumer welfare, may also come from regulatory failure.[191] *Personal detriment* arises from the 'negative outcomes that consumers experience once a purchase is made, relative to some benchmark such as reasonable expectations' − comparing actual value received versus value reasonably expected (or promised).[192] As such, personal detriment affects *individual* consumers.

Detriment suffered can be *financial* or *non-financial* and either *apparent* or *hidden*. As previously noted, financial detriment is usually apparent and relatively straightforward to rectify with existing consumer protections. Non-financial detriment such as negative psychological outcomes, compromise of personal information, or adverse effects on physical health are far more difficult for both individuals to determine, and regulators to rectify, as these often present as *hidden* detriment.[193] This is particularly the case with goods and services high in credence attributes such as DTCGT, which must be accepted 'on trust' as substantive evaluation is generally not possible even after consumption.[194] In most instances the transaction costs of evaluating and validating credence attributes are prohibitive in relation to marginal benefits, even if such information was available.

Emotions play an important role in the consumption experience, shaping and giving it meaning.[195] Emotional responses even to the same consumption experience can vary depending on individual differences and circumstances, making them challenging to both define and measure.[196] Emotional responses can be a source of consumer detriment in their own right, but also function as a precursor to longer-term psychological detriment. Longer- term psychological detriment can have cognitive, affective and behavioural consequences, causing confusion, reduced self-confidence, and regret relative to past consumer decisions thereby influencing future decisions.

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<https://eprints.soton.ac.uk/148227/1/The_Psychology_of_Consumer_Detriment.pdf>; Europe Economics, *An analysis of the issue of consumer detriment and the most appropriate methodologies to estimate it: Final Report,* (2007), 3 <http://www.europe-economics.com>.

[191] Europe Economics, *An analysis of the issue of consumer detriment and the most appropriate methodologies to estimate it: Final Report*, (2007), 3 <http://www.europe-economics.com>.

[192] OECD, *Consumer Policy Toolkit* (2010) OECD Publishing, DOI: 10.1787/9789264079663-en, 52.

[193] Ibid 54-55; Commonwealth of Australia, *Consumer policy in Australia: A companion to the OECD Consumer Policy Toolkit* (2011) 20 <http://consumerlaw.gov.au/files/2015/09/Companion_to_OECD_Toolkit.pdf>.

[194] Michael Darby and Edi Karni, 'Free Competition and the Optimal Amount of Fraud' (1973) 16 *Journal of Law and Economics*, 67-88.

[195] Peter Lund, Laura Miller, Johanna Körting and Joseph Ungemah, *The psychology of consumer detriment: A conceptual review* (2006) Office of Fair Trading OFT792, 65 <https://eprints.soton.ac.uk/148227/1/The_Psychology_of_Consumer_Detriment.pdf>.

[196] Lund et al. provide a useful overview of the complexity of the psychological literature defining emotions.

The long-term impact of strong negative emotional reactions has also been shown to adversely affect physical well-being.[197] As such, the effects of hidden and in particular psychological detriment may take time to present and even when presenting may not be obviously linked with specific consumer purchases.

While consumer detriment and causation can be difficult to measure and its effects may take time to present, a range of methodologies such as focus groups, surveys, econometric analysis, and analysis of consumer complaints can be used.[198] Each of these however has both advantages and disadvantages – for example, analysis of consumer complaints depends on a sufficient number of consumers lodging complaints, while focus groups represent the views of a small number of individuals.

## CONCLUSION

This chapter modelled the pathways, processes and protections afforded *patients* pursuing CGT and *consumers* pursuing DTCGT. In the CGT pathway with its medical, quality and financial gatekeepers, the potential exists for *protracted translation* of genetic discoveries into available clinical treatments. However, given the commercial imperative driving the DTCGT pathway, the potential exists for *premature translation*, with the time from lab to market becoming increasingly shorter. The former denies individuals what may be life saving or altering treatments, while the latter may expose individuals to unsubstantiated science resulting in either wasted money or potentially harmful outcomes.

While the paradigm shift from *medical* to *consumer* is obvious, modelling identified the potential for CGT and DTCGT pathways and processes to merge, with some of the protections provided for CGTs also applying to DTCGTs in Australia. When these pathways and processes merge through consumer or company-initiated engagement with healthcare, individuals' roles change from *consumer* to *patient*, providing traditional protections afforded in the CGT pathway. Adding to the complexity is the additional role of *research participant* if *consumers* agree to participate in DTCGT company research.

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[197] See Richard Suinn, 'The Terrible Twos—Anger and Anxiety: Hazardous to Your Health' (2001) 56 *American Psychologist* 27-36.

[198] For example, UK Department of Business Innovation & Skills (2014), *Consumer Engagement and Detriment Survey*, HM Government, London; Consumer Affairs Victoria (2006), *Consumer detriment in Victoria: a survey of its nature, costs and implications*, Government of Victoria, Melbourne. For a comprehensive discussion of methodologies, see Europe Economics (2007), *An analysis of the issue of consumer detriment and the most appropriate methodologies to estimate it: Final Report,* Europe Economics, London <http://www.europe-economics.com>.

In the medical space, Medicare and the TGA determine the analytic validity of CGTs while Medicare and NATA ensure clinical validity. Clinical utility is determined generally by Medicare in terms of genetic test availability, with patient-specific clinical utility determined by medical professionals and genetic specialists. In the commercial space, the analytic and clinical validity of DTCGTs is dependent on the science the day, with clinical validity the responsibility of laboratories, which may or may not be accredited. Clinical utility is the responsibility of individuals who firstly decide to purchase tests and ultimately interpret results determining what, if anything, they will do in response. During the DTCGT process, consumers make significant assumptions – assuming tests conducted and results provided are accurate, and that they have interpreted and actioned them in appropriate ways. Self-interpretation of genetic results however has the potential to generate 'false positives' and 'false negatives' each leading to potential personal, non-financial detriment.

Chapter Four investigates some of the concerns expressed in the academic literature, position statements and organisational or government reports to further clarify the problem identification stage relative to the DTCGT offering, its impact on individuals, and its impact on the healthcare system. Chapter Four also provides guidance for the survey component, which will focus specifically on *personal non-financial detriment*, especially that which may be *hidden*.

# Chapter Four:

# DTCGT: potential for consumer harm or 'monsters under the bed'?

# INTRODUCTION

*'DTCGT companies say they are empowering people to take control of their health and their future. But it's really a commercial transaction …'*[1]

The previous two chapters have illustrated that both genetic testing and the space within which it operates, whether medical or commercial, are extremely complex. While proponents of DTCGT have focused on its promise to ***empower consumers*** – that rational, self-governing individuals who have the right to access their personal genetic data will proactively use it in healthcare decision-making – not all agree. While acknowledging the promise, a large number of metaphorical 'monsters under the bed' have been identified – issues of significant concern and sufficiently serious to require regulation.[2] When the expansive body of academic commentary, government and organisational reports, and mass media coverage is viewed holistically, the overarching concern remains the ***potential for consumer harm***, especially so if consumers use test results to make significant independent treatment, prevention and lifestyle decisions. Such harm, it is suggested, has the potential to turn healthy individuals who have no real concerns into the genetically 'worried well',[3] generate unjustified levels of anxiety or encourage inappropriate behaviours in those who should only be slightly concerned, or worse, falsely reassure individuals who should be very concerned and seek immediate medical attention.

Moving genetic testing into the online environment market is undoubtedly redefining healthcare roles as discussed in Chapter Three, making consumers active rather than passive participants in healthcare decision-making. The DTCGT industry's commodification and monetisation focus has imbued genetic data with economic value. As consumer demand increases, the potential for consumer harm, especially psychological harm, resulting from the potential premature translation of genetic discoveries into for-profit tests, if it exists, would also be expected to increase. The commercial imperative driving DTCGT companies would dictate adding tests to bundled offerings as soon as the science is available is precisely what they *should* and *would* do – in the absence of

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[1] Anon, 'Direct-to-Consumer genetic test results can be lost in translation' ePathWay, The Royal College of Pathologists of Australasia (2012) Issue 011. <http://epathways.rcpa.edu.au/one.html>. Quoting Dr Graeme Suthers, then Chair of the RCPA Genetics Advisory Committee.

[2] See Timothy Caulfield, Subhashini Chandrasekharan, Yann Joly and Robert Cook-Deegan, 'Harm, hype and evidence: ELSI research and policy guidance' (2013) 5(21) *Genome Medicine* <http:genomemedicine.com/content/5/2/21>; Pascal Borry, Rachel van Hellemondt, Dominique Sprumont, Camilla Jales, Emmanuelle Rial-Sebbag, Tade Spranger, Liam Curren, Jane Kaye, Herman Nys and Heidi Howard, 'Legislation on direct-to-consumer genetic testing in seven European countries' (2012) 20 *European Journal of Human Genetics* 715-721.

[3] Jessica Cussins, 'Direct-to-consumer genetic tests should come with a health warning' (2015) 294(7845) The Pharmaceutical Journal DOI: 10.1211/PJ.2015.20067564.

anything saying they *can't* ... regardless of whether tests have ultimately been validated and proven useful.

The established body of empirical studies of actual and potential consumers primarily in the US and emerging Australian research have investigated whether the concerns identified are evident in consumers' engagement with DTCGT. These studies help to shine a metaphorical 'light under the bed', allowing for confirmation, quantification, and contextualisation, in essence helping to determine if the 'monsters' identified are real, their significance, and whether consumers should be worried.

This chapter does not focus on theoretical concepts underlying DTCGT, but seeks to match expressed concerns with empirical research, applying a consumer behaviour lens to identify areas where more research is necessary.[4] While the concerns that have been raised are numerous, not all could be tested in the survey component of this research. Several issues relative to the DTCGT offering, its impact on consumers, and its impact on the healthcare system were selected for inclusion as they represented key aspects of the DTCGT process in the researcher's judgement. As such, this chapter reports only on concerns fundamental to the development of the survey instrument used to assess the potential for consumer detriment and is organised into three parts.[5]

Part One reviews concerns about the DTCGT offering itself focusing on the DTCGT validity, terms of service and privacy policies governing the legally binding contract between consumer and company, and the marketing practices engaged in by DTCGTs to encourage purchase.

Part Two reviews concerns about DTCGT's impact on consumers, exploring how they interpret personal test information, resulting psychological outcomes and behavioural intentions, and the sharing of genetic information with family, online, and as part of company research. Of key

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[4] See Jan Charbonneau, Michael Solomon, Greg Marshall and Elnora Stuart, *Marketing: Real People, Real Choices* 2nd ed. (Pearson New Zealand, 2011), Chapter 2 Consumer and Organisational Behaviour.

[5] Important aspects of the DTCGT debate such as ethics, the contentious issue of testing of minors, genetic discrimination and whether genetic information should have special status in law are beyond the scope of this research. See Pascal Borry, 'Direct-to-consumer genetic testing: from ethical concerns to policy answers' (2013) 6(3) *Bioethics* 114-117; Nathalie Moray, Katherina Pink, Pascal Borry and Maarten Larmuseau, 'Paternity testing under the cloak of recreational genetics' (2017) 25 *European Journal of Human Genetics* 768-770; Margaret Otlowski, Sandra Taylor and Yvonne Bombard, 'Genetic discrimination: international perspectives' (2012) 13 *Annual review of genomics and human genetics* 433-454; Australian Law Reform Commission and Australian Health Ethics Committee, *Essentially Yours: Protection of the Human Genetic Information in Australia*, Report No 96 (2003).

concern is potential for unjustified anxiety from false positive results and false reassurance from false negative results, whether resulting from test issues or consumer interpretation.[6]

Part Three investigates DTCGT's impact on the healthcare system, focusing on both consumer-initiated and company-initiated sharing with healthcare professionals, and whether healthcare professionals themselves feel prepared if and when presented with DTCGT test results.

# PART ONE: CONCERNS ABOUT THE DTCGT OFFERING

Part One looks specifically at three key areas of concern that have featured prominently in the DTCGT discourse: the validity of tests offered, contractual terms forming the basis of the consumer/company relationship, and marketing practices used to encourage DTCGT purchase.

## *4.1.1 DTCGT tests: Valid or premature?*

The following section discusses how DTCGT is conducted and quality issues involving analysis of single nucleotide polymorphisms (SNPs).[7]

### *4.1.1.1 How is DTCGT conducted?*

Unlike CGT where specific tests are ordered in response to specific assessed needs (targeted testing), DTCGT's core business model is based on bundled testing. A panel of tests including health-related are conducted and results returned en masse to consumers (non-targeted testing).[8] DTCGT companies decide the specific tests to offer in their bundles, which consumers either 'take or leave'. Consumers receiving results from these bundled tests are left to identify which results they believe are personally relevant, and which they choose to ignore.[9]

While some do offer whole genome and exome sequencing, most DTCGT companies focus on single nucleotide polymorphisms (SNPs) in their test offerings, relying on the 'science of the day' to identify SNPs of interest. Testing involves comparing SNPs from consumers' DNA with reference sequences identified in published scientific research and genome-wide association

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[6] Giuseppe Lippi, Emmanuel Favaloro and Mario Plebani, 'Direct-to-consumer testing: more risks than opportunities' (2011) 65(12) *International Journal of Clinical Practice* 1121-1229.
[7] As noted in Chapter One, whole genome and exome sequencing offered by DTCGT companies is not discussed in this research.
[8] See Eline Bunnik, Maartje Schermer and Cecile Janssens, 'Personal genome testing: Test characteristics to clarify the discourse on ethical, legal and societal issues' (2011) *BMC Medical Ethics* DOI: 10.1186/1472-6939-12-11.
[9] See Anon, 'Direct-to-Consumer genetic test results can be lost in translation' ePathWay, The Royal College of Pathologists of Australasia (2012) Issue 011, February <http://epathway.rcpa.edu.au/one.html>.

studies (GWAS), as discussed in Chapter Two (2.1.5.2 SNPs; 2.2.5 GWAS). These reference SNPs are associated with disease risk and are used to calculate the individual's *probability* of developing each disease tested.[10] Extracted DNA is first amplified (copied), spliced into sections, tagged with fluorescent markers and then placed on microarrays containing millions of small DNA sections complementary to each SNP being analysed (probes). Tagged sections then pair with complementary probes according to DNA's precise pairing rules (e.g. A only pairs with T), indicating whether SNPs under investigation are present. The more SNPs included for each disease, the more refined the predictive test; although GWAS have shown most identified SNPS are statistically associated with only low to moderate risk.[11]

### *4.1.1.2 Test quality*

*'Massive-scale testing of thousands of single-nucleotide polymorphisms (SNPs) is not error free, and such errors could translate into misclassification of risk.'*[12]

Given the accelerating pace with which genetic testing is evolving, questions have been raised about the quality and value of both CGT and DTCGT, with commentators questioning test accuracy, links between increased predisposition and disease development, and whether treatment or lifestyle changes exist to mitigate or at least manage indicated risk.[13] One primary concern noted in Chapter Three (3.6.1.1) is the potential for premature translation in the DTCGT space. DTCGT companies have both the ability and commercial imperative to make tests available as soon as possible after SNPs are identified, compared to the more conservative, potentially protracted translation in regulated and gatekeepered healthcare systems.

As most DTCGT tests indicate probabilities only, if the tests themselves (or the SNPs tested) are not accurate, the chance of unjustified anxiety from consumer interpretation of false positive test results and false reassurance from false negative results increases.[14] With bundled testing, inaccuracies can occur for individual tests, creating a multiplier effect when the individual

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[10] Thierry Frebourg 'Direct-to-consumer genetic testing services: what are the medical benefits?' (2012) 20 *European Journal of Human Genetics* DOI: 10.1038/ejhg.2011.229.
[11] Brandie Heald, Emily Edelman and Charis Eng, 'Prospective comparison of family medical history with personal genome screening for risk assessment of common cancers' (2012) 20 *European Journal of Human Genetics* 547-551.
[12] Kenta Imai, Larry Kricka and Paolo Fortina, 'Concordance Study of 3 Direct-to-Consumer Genetic-Testing Services (2011) 57(3) *Clinical Chemistry* 518-521, 518.
[13] See Rachel Kalf, Raluca Mihawscu, Suman Kundu, Peter de Knijff, Robert Green and Cecile Janssens, 'Variations in predicted risks in personal genome testing for complex diseases' (2013) *Genetics in Medicine* DOI:10.10.1038/gim2013.80.
[14] Giuseppe Lippi, Emmanuel Favaloro and Mario Plebani, 'Direct-to-consumer testing: more risks than opportunities' (2011) 65(12) *International Journal of Clinical Practice* 1121-1229.

considers all results together. Further, these tests only consider one piece of the 'disease puzzle' as lifestyle and family history are not factored in, calling their predictive ability into question.[15] In CGT, the effectiveness of family history based assessment for determining risk is widely acknowledged and plays a key role in needs assessment.[16] Research by Bloss et al. found DTCGT risk information for high heritability diseases as accurate as traditional risk predictions using family history alone. Heald et al. however, found the opposite, again suggesting the variability and possibly limited additional value of DTCGT.[17]

#### *4.1.1.3 How are DTCGT tests developed?*

While some DTCGT companies develop tests based on the results of their own research, most rely heavily on the peer-reviewed science to identify associations and SNPs to test. One such source is the publicly accessible ClinVar database launched in 2013 by the US National Centre for Biotechnology Information in the NIH (www.ncbi.nim.nih.gov/clinvar). ClinVar was created as the primary site for researchers, laboratories, experts, clinicians, and patients to deposit and retrieve variants and any provided supporting evidence, with risk predictions changing as new variants are added. By 2015, while more than 80 million genetic variants had been discovered; the role of the majority still remains unclear.[18] This database, coupled with published academic research studies and GWAS provides ready access to the science of the day for all – including DTCGT companies.

Database analysis conducted in 2015 found multiple interpretations of the same variant, over 400 of which would have a 'differential effect on medical decision making', with subsequent evidence requiring reclassification e.g. from pathogenic to likely benign.[19] This suggests today's science could be obsolete tomorrow, or more worryingly wrong, given the exponential rate of genetic

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[15] Cecile Janssens, A Wilde and I van Langen, 'The sense and nonsense of direct-to-consumer genetic testing for cardiovascular disease' (2011) 19 *Neth Heart J* 85-88.
[16] Brandie Heald, Emily Edelman and Charis Eng, 'Prospective comparison of family medical history with personal genome screening for risk assessment of common cancers' (2012) 20 *European Journal of Human Genetics* 547-551.
[17] Cinnamon Bloss, Eric Topol and Nicholas Schork, 'Assocation of Direct-to-Consumer Genome-Wide Disease Risk Estimates and Self-Reported Disease' (2012) 36 *Genetic Epidemiology* 66; Brandie Heald, Emily Edelman and Charis Eng, 'Prospective comparison of family medical history with personal genome screening for risk assessment of common cancers' (2012) 20 *European Journal of Human Genetics* 547-551.
[18] Heidi Rehm, Jonathan Berg, Lisa Brooks, Carlos Bustamante, James Evans, Melissa Landrum et al, 'ClinGen – The Clinical Genome Resource' (2015) 372(23) *New England Journal of Medicine* 2235-2242.
[19] Ibid 2240.

discoveries. As such, risk predictions may change too frequently to be of any practical utility – especially concerning given DTCGT's potential for premature translation.[20]

#### *4.1.1.4 Are DTCGT tests valid?*

Analytic and clinical validity of DTCGT tests has been questioned in several studies, with concerns echoed in organisational reports, position statements and government guidelines.[21] Australia's National Health and Medical Research Council (NHMRC) and Royal College of Pathologists advised DTCGTs might not have the analytic and clinical validity expected of CGTs, with the Human Genetics Society cautioning consumers as to the variability of results from different companies.[22]

Illustrative of this variability is the US Government Accountability Office (GAO) 2010 study finding divergent results from multiple DTCGT companies testing the same DNA samples. Inconsistent risk estimates between companies, and results conflicting with medical histories of DNA donors, led the GAO to conclude results were of 'little or no practical use' to consumers.[23] Also noted were how results were phrased and contextualised. One 'consumer' in the investigation who received an above average risk prediction for breast cancer was told that meant she was at 'high risk of pretty much getting' the disease.

Subsequent investigation revealed that while individual SNPs may be clinically valid, companies decide which GWAS results to use, leading to variation in specific SNPs and number tested, quantitative risk formulae applied, and average lifetime risk percentages used.[24] GWAS themselves may have uncertain clinical validity due to 'limited and potentially biased study

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[20] See Laura Kurtzman, 'Multi-gene test predicts Alzheimer's better than APOE E4 alone' 22 September 2017 *UCSF News* <https://www.ucsf.edu/news/2017/09/408356/multi-gene-test-predicts-alzheimers-better-apoe-e4-alone>.

[21] See European Academies Science Advisory Council, Direct-to-consumer genetic testing for health-related purposes in the European Union (2012); UK Human Genetics Commission, More Genes Direct (2007) and Genes Direct (2003).

[22] Human Genetics Society of Australasia, Position Statement: Online DNA testing (2018) <https://www.hgsa.org.au/documents/item/18>; Australian Government, NHMRC, *Understanding direct-to-consumer genetic DNA testing: An information resource for consumers* (2014); Australian Government, NHMRC, *Discussing direct-to-consumer genetic testing with patients: A short guide for health professionals* (2013) <http:www.nhmrc.gov.au>; Anon, 'Direct-to-Consumer genetic test results can be lost in translation' ePathWay, The Royal College of Pathologists of Australasia (2012) Issue 011, February, <http://epathway.rcpa.edu.au/one.html>.

[23] Gregory Kutz, 'Direct-to-consumer genetic tests: misleading test results are further complicated by deceptive marketing and other questionable practices' (2010) <https://www.gao.gov/assets/130/125079.pdf>.

[24] See Rachel Kalf, Raluca Mihawscu, Suman Kundu, Peter de Knijff, Robert Green and Cecile Janssens, 'Variations in predicted risks in personal genome testing for complex diseases' (2013) *Genetics in Medicine* DOI:10.10.1038/gim2013.80; Kenta Imai, Larry Kricka and Paolo Fortina, 'Concordance study of 3 direct-to-consumer genetic testing services' (2011) 57(3) *Clinical Chemistry* 518-521.

populations' and their focus only on genetic factors.[25] While researchers seek more ethnically diverse samples, GWAS results primarily represent Caucasian samples of European descent, a fact often not mentioned to consumers in DTCGT marketing.[26]

A 2018 study analysing a small number of DTCGT raw data files sent for confirmation testing found 40% of variants identified were false-positives, with some 'increased risk' variants reclassified as benign. The authors noted DTCGT companies and third party interpretation services do not always update tests when new variants are discovered. They found, for example, 23andMe's Parkinson's test did not include variants *SNCA* and *PARK2/PARKIN* identified in 2015.[27] In response, 23andMe pointed out the challenges of determining causal relationships between genetic variants and disease were not unique to DTCGT but applied to the entire genetic testing industry, and their health reports have 'proven accuracy through FDA authorisation' against analytic validity requirements for DTCGT tests that are higher than those for many clinical tests – both valid points.[28]

Clinical, and indeed personal, utility depends on consumers fully understanding disease risks identified and using results appropriately in informed healthcare decision-making.[29] Even assuming analytic and clinical validity, the potential for unjustified anxiety or false reassurance always exists from consumer interpretations.[30] Early research suggested many consumers questioned their own ability to interpret results, stating their intention to seek assistance and advice from healthcare professionals.[31]

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[25] Susanne Haga, Muin Khoury and Wylie Burke, 'Genomic profiling to promote a healthy lifestyle: not ready for prime time' (2003) 34(4) *Nature* Genetics 347-380, 348.
[26] Sarah Zhang, '23andMe wants its DNA database to be less white' (2018) 23 April *The Atlantic* <https://www.theatlantic.com/science/archive/2018/04/23andme-diversity-dna/558575/>. To enhance the diversity of its data, 23andMe provides free test kits to Asian and African researchers.
[27] Stephany Tandy-Connor, Jenna Guiltnan, Kate Krempely, Holly LaDuca, Patrick Reineke, Stephanie Gutierrez, Phillip Gray and Brigette Tippin Davis, 'False-positives results released by direct-to-consumer genetic tests highlight the importance of clinical confirmation testing for appropriate patient care' (2018) *Genetics in Medicine* DOI: 10.1038/glm.2018.38.
[28] Shirley Wu, Jeffrey Pollard, Arnab Chowdry, Richard Scheller and Robert Gentleman, 'Addressing the accuracy of direct-to-consumer genetic testing' (2018) *Genetics in Medicine* <https://www.nature.com/articles/s41436-018-0094-5>.
[29] See Mary-Claire King, Ephrat Levy-Lahad and Amnon Lahad, 'Population-based screening for BRCA1 and BRCA2' (2014) 312(11) *JAMA* DOI: 10.1001/jama.2014.12483.
[30] See Rebecca Mathews, Wayne Hall and Adrian Carter, 'Direct-to-consumer genetic testing for addiction susceptibility: a premature commercialisation of doubtful validity and value' (2012) 107 *Addiction* 2069-2074.
[31] See Amy McGuire, Christina Diaz, Tao Wang and Susan Hilsenbeck, 'Social Networkers' Attitudes Toward Direct-to-Consumer Personal Genome Testing' (2009) 9(6-7) 3-10.

#### 4.1.1.5 DTCGT's inherent limitation

*'If I were to pull a book off the shelf and I read the first letter on every three pages … I wouldn't know if I was reading the phone book or Tolstoy.'*[32]

And that, paraphrasing Hamlet, is the rub. Most DTCGT companies analyse SNPs only – individual letters. And like all genetic tests, they provide information only concerning the genetic component of disease, and that will always be their inherent limitation.[33] Given 'only relatively small number of common variants involved have been identified and their effect sizes are generally low... most tested individuals have predicted risks that are very close to average', limiting actionability and calling into question their value as a tool of consumer empowerment.[34]

### 4.1.2 Contract terms: Is data the new consideration[35]

DTCGT is a commercial offering resulting in a commercial transaction, with the contract governing the transaction between consumer and company.[36] As most DTCGT companies operate online, their contracts are e-contracts which, to be legally binding, must comply with standard contract requirements.[37] As with all contracts, acceptance of terms and conditions is deemed once signed, whether contracts are read or not, as confirmed by the High Court in *Toll (FCGT) Pty Ltd v Alphapharm Pty Ltd (2004)* 219 CLR 165.[38]

DTCGT contracts are standard-form contracts where all terms and conditions are set by companies, with consumers unable to negotiate or opt out of specific conditions. Contracts govern everything from testing, sharing and storage of genetic and personal information, to

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[32] Kaomi Goertz, 'Korean adoptees are using DNA kits to get a glimpse of their ancestry' 21 July 2015 www.pri.org <https://www.pri.org/stories/2015-07-21/korean-adoptees-are-using-dna-kits-get-glimpse-their-ancestry>. Quoting Robert Klitzman, Director of Masters of Bioethics, Columbia University (US).

[33] See Amanda Field, Alyson Krokosky and Sharon Terry, 'Direct-to-Consumer Marketing of Genetic Tests: Access Does Not Reflect Clinical Utility' (2010) 14(6) *Genetic Testing and Molecular Biomarkers* 731-732.

[34] Cecile Janssens, A Wilde and I van Langen, 'The sense and nonsense of direct-to-consumer genetic testing for cardiovascular disease' (2011) 19 *Neth Heart J* 85-88, 86.

[35] A contract is a legally binding promise or agreement. Consideration, an essential element for enforceability, is the exchange of one thing of value for another. For further information, see Jeannie Paterson, Andrew Robertson and Arlen Duke, *Principles of Contract Law* 5e (Lawbook Co., 2016) Chapter 4. Consideration is determined by contract parties and must be sufficient but need not be adequate. See *Woolworths Ltd v Kelly* (1991) 22 NSWLR 189.

[36] See Andelka Phillips, 'Genomic privacy and direct-to-consumer genetics (2015) *IEEE* DOI: 10.1109/SPW.205.19.

[37] *Electronic Transactions Act 1999* (Cth) and companion state and territory legislation. Offer/acceptance (certainty of terms); consideration; capacity; intention to be bound.

[38] See Andelka Phillips, 'Think before you click: Ordering a genetic test online' (2015) 11(2) *TheSciTech Lawyer* <https://www.americanbar.org/publications/scitech_lawyer/2015/winter/think_before_you_click_ordering_genetic_test_online.html>.

copyright and intellectual property. Phillips noted their extensive length in her extensive review, with 23andMe's Terms of Service at 9081 words and its Privacy Policy 15805 words.[39] Further, Phillips found a large number of contracts where agreement was deemed, often simply through website viewing, with many retaining the right to change terms at will.[40]

Click-wrap contracts, where consumers accept or decline via digital prompt, have become ubiquitous in the online world with an average consumer entering 'more contracts in a year than their grandparents did in a life-time.'[41] Given this volume, it has been suggested online consumers have become habituated to clicking without reading.[42] Even if read, consumers often overlook the most obvious of conditions. This psychological phenomenon is known as inattentional blindness.[43] Early analysis of DTCGT websites found wide variability relative to content and usability. One study found the average reading level of websites at grade 15, the equivalent of 15 years of formal education, compared to the recommended grade 7-8.[44] These high literacy demands suggest users would likely struggle to both find and understand important legal information.[45]

Many DTCGT companies state they are providing test results for 'research, education and information purposes only' and encourage consumers to seek advice from healthcare professionals. Commentators have questioned whether consumers understand such disclaimers and realise DTCGT test results do not represent a medical diagnosis. Early research would suggest not, with one study finding a third of respondents considered DTCGT a diagnosis.[46] Whether such disclaimers would be considered effective has not yet been determined in the courts. However,

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[39] Andelka Phillips, 'Reading the fine print when buying your genetic self online: direct-to-consumer genetic testing terms and conditions' (2017) 36(3) *New Genetics and Society* 273-295.
[40] Andelka Phillips, 'Genomic privacy and direct-to-consumer genetics" (2015) *IEEE* DOI: 10.1109/SPW.205.19.
[41] Andelka Phillips, 'Reading the fine print when buying your genetic self online: direct-to-consumer genetic testing terms and conditions' (2017) 36(3) *New Genetics and Society* 273-295, 273.
[42] See Nancy Kim, *Wrap contracts: foundations and ramifications* (Oxford University Press, 2013).
[43] See Siri Carpenter, 'Sights unseen' (2001) 32(4) *American Psychological Association Monitor* <http://www.apa.org/monitor/apr01/blindness.aspx>. As an example, in 2017 UK Internet provider *Purple* added clauses to its agreement such as the commitment to 'clean public toilets' with 20,000 accepting terms with only one reporting clauses over its 2 week experiment. David Tuffley, 'How not to agree to clean public toilets when you accept any online terms and conditions', 24 July 2017 *The Conversation* <https://theconversation.com/how-not-to-agree-to-clean-public-toilets-when-you-accept-any-online-terms-and-conditions-81169>.
[44] See National Library of Medicine, 'How to write easy-to-read health materials' (2016) <https://medlineplus.gov/etr.html>.
[45] Christine Lachance, Lori Erby, Beth Ford, Vincent Allen, Kimberly Kaphingst, 'Informational content, literacy demands, and usability of websites offering health-related genetic tests directly to consumers' (2010) 12(5) *Genet Med* 304-312, 304.
[46] Amy McGuire, Christina Diaz, Tao Wang and Susan Hilsenbeck, 'Social Networkers' Attitudes Toward Direct-to-Consumer Personal Genome Testing' (2009) 9(6-7) *Am J Bioeth* 3-10, 7.

the Royal College of Pathologists of Australia in its 2018 position statement noted labelling the test as such did not change its nature, suggesting such tests should not be marketed directly to consumers.[47]

Contracts are legal documents written in complex legal language, often with extensive exclusion clauses. Of debate is whether consumers are able to able to fully understand DTCGT contract terms, in particular jurisdictional clauses and property rights clauses.[48] Jurisdictional clauses dictate which country's law applies, with companies often selecting jurisdictions with limited consumer protection. As such the domestic laws that provide consumers with confidence and protection in local marketplace transactions may be of little or no assistance, especially in cases of dispute.

DTCGT contracts typically contain waiver of property rights clauses. Property refers to a right, interest or thing of value, legally capable of ownership.[49] Whether individuals have legally enforceable property rights, and therefore ownership, in their DNA and exclusive authority to determine its use has not as yet been definitively determined in any common law court. Insight can be gained from cases such as *Moore v Regents of the University of California* 793 P.2d 479 (Cal. 1990) where the argument for individual rights in cells was rejected. In *Washington University v Catalona* 409 F.3d 667 (8th Cir.2007), it was determined individuals donate biospecimens for research as *inter vivos* gifts (voluntary donations that cannot be revoked), thereby retaining no property rights. In Australia, it is illegal to sell bodies and parts suggesting no property rights, although these can be gifted or donated with informed consent suggesting some form of control. Insertion of these clauses into DTCGT contracts functions as 'future proofing' – if property rights in DNA are ultimately established, individuals have already waived such rights. Consumers' DNA sent in for specific analysis *could* therefore be monetised by DTCGTs through

[47] The American College of Medical Genetics and Genomics, 'Direct-to-consumer genetic testing: a revised position statement of the American College of Medical Genetics and Genomics; (2016) 18(2) *Genetics in Medicine* 207-208; The Royal College of Pathologists of Australasia, Position Statement: Genetic tests that are marketed directly to consumers (2013) No. 2 <https://www.rcpa.edu.au/getattachment/2be86825-4c53-4d47-84ec-a2730954b021/Genetic-Tests-that-are-Marketed-Directly-to-Consum.aspx>.

[48] Ian Ayres, 'The no-reading problem in consumer contract law' (2014) 66(545) *Yale University Faculty Scholarship Series* Paper 4872 <http://digitalcommons.law.yale.edu/fss_papers/4872>.

[49] LexisNexis, *Concise Australian Legal Dictionary* 5th ed (LexisNexis Butterworths, 2015). While only tangentially related, in *Yanner v Eaton* [1999] HCA 53, the High Court considered the Crown's property rights in fauna, determining 'property' does not necessarily mean full, beneficial or legal ownership but could have varying degrees of intensity. Whether this same reasoning would be applied to DNA remains to be determined.

sale of genetic data or its use in development of commercial products, with no potential for benefit sharing.[50]

#### *4.1.2.1 Genetic privacy*

*'Healthcare data is now more valuable to cyber crooks than credit card or social security numbers.'*[51]

Genetic information by its very nature is the most personal of information, not just about individuals but extended families, with its unique nature recognised in non-binding but nonetheless normative international agreements.[52] Each time individuals share genetic data an opportunity is presented for inadvertent or deliberate privacy breaches.[53] Genetic information from DTCGT results or raw data files, especially when combined with online search data and medical information volunteered through online sharing, is extremely valuable and ripe for monetisation – and misuse. And unlike iTunes passwords, if genetic data is disclosed, it cannot be changed.[54]

In Australia, genetic information is protected through the *Privacy Act 1988* (Cth) rather than a separate statutory regime.[55] Schedule 1 of the Act outlines the Australian Privacy Principles (APP) dictating how government agencies, private health services providers and private sector companies with turnover over $3million must handle personal information.[56] A small business exemption for entities with under $3million annual turnover exists however not if they are health

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[50] See Anna Harris, Sally Wyatt and Susan Kelly, 'The gift of spit (and the obligation to return it)' (2013) 16(2) *Information, Communication & Society* 236-257; Amanda Singleton, Lori Erby, Kathryn Foisie and Kimberly Kaphingst, 'Informed Choice in Direct-to-consumer Genetic Testing (DTCGT) Websites: A Content Analysis of Benefits, Risks and Limitations' (2012) 21 *Journal of Genetic Counseling* 433-439. It must be noted 'no benefit sharing' is also common in clinical medical trials and biobanking.

[51] Byron Connolly, 'Medical data more valuable to hackers than credit information' (2018) 23 July <https://www.cio.com.au/article/644161/medical-data-more-valuable-hackers-than-credit-information/>.

[52] See UNESCO, *Universal Declaration on the Human Genome and Human Rights* (1997), and UNESCO, *International Declaration on Human Genetic Data* (2003).

[53] See Xinghua Shi and Xintao Wu, 'An overview of human genetic privacy' (2017) 1387(1) 61-72; Yanic Erlich and Arvind Narayanan, Routes for breaching and protecting genetic privacy' (2014) 15(6) *Nat Rev Genet* 409-421.

[54] Andelka Phillips and Jan Charbonneau, '*Giving away more than your genome sequence:* Privacy in the Direct-to-Consumer Genetic Testing Space' (2016) *PrivacyCon*, Federal Trade Commission, Washington DC, US.

[55] Privacy refers to protecting against unwanted interference or public scrutiny. The Act gives partial force to Australia's obligations under the *International Covenant on Civil and Political Rights 1966.* See Article 17 (1) 'No one shall be subjected to arbitrary or unlawful interference with his privacy…'

[56] The *Privacy Amendment (Enhancing Privacy Protection) Act 2012* amended the *Privacy Act 1988* (Cth) to include the thirteen Australian Privacy Principles (effective 12 March 2014).

services providers (s6D).[57] Health services include activities performed to assess, record, maintain or improve health and diagnosis or treat actual or suspected illness or disability.[58] While these principles would cover healthcare professionals and larger DTCGT companies, it is unclear whether smaller turnover DTCGTs would be able to avail themselves of the small business exemption which would depend on whether they were deemed as health service providers.[59]

Health information is deemed sensitive information, with predictive genetic information specifically included.[60] Sensitive information may only be collected if reasonably necessary and informed consent is obtained, with use forbidden for purposes beyond which it was collected.[61] In recognition of the familial nature of genetic information, an exemption was created to an individual's right to privacy over their genetic information. The *Privacy Legislation Amendment Act 2006* (Cth) changed 95AA of the *Privacy Act 1988* (Cth) to allow health practitioners to disclose genetic information *without consent* in circumstances of serious risk to genetic relatives. Whether health practitioners have a legal duty to make such a disclosure however has not been judicially determined in Australia.

Questions have been raised as to whether these overarching privacy principles are sufficient when genetic information enters the commercial realm.[62] DTCGT companies, online interpretation sites, and online sharing platforms each have their own privacy policies and terms of service, with most considering data sharing as consideration in exchange for website use.

Analysis of the privacy policies of Australian DTCGT companies found many companies non-compliant with the APPs, with special attention needed with respect to use and disclosure relative to research and third parties.[63] Similar results were found in the US with DTCGT companies falling

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[57] *Privacy Act 1988* (Cth) Part II Division 1 s6D.
[58] Ibid 1 s6.
[59] Dianne Nicol, Meredith Hagger, Nola Ries and Johnathon Liddicoat, 'Time to get serious about privacy policies: The special case of genetic privacy' (2014) *Federal Law* Review 42(1) 149-179.
[60] *Privacy Act 1988* (Cth) Part II Division 1 s6. Genetic information must be 'in a form that is, or could be, predictive of the health of the individual or a genetic relative of the individual.' See also Schedule 1 Part 2 Collection of Personal Information relative to solicited and unsolicited personal information and Schedule 3, Principle 10 dealing with sensitive information.
[61] See also *Privacy Act* 1988 (Cth) Schedule 1 Part 2 Collection of Personal Information relative to solicited and unsolicited personal information (Principles 3 and 4) and Schedule 3, Principle 10 dealing with sensitive information.
[62] See Hsiao-Ying Huang and Masooda Bashir, 'Direct-to-consumer genetic testing: Contextual privacy predicament' (2015) *ASIST* 1- 10; Sandra Soo-Jin Lee and Emily Borgelt, 'Protecting posted genes: Social networking and the limits of GINA' (2014) 14(11) *Am J Bioeth* 57-59.
[63] Dianne Nicol, Meredith Hagger, Nola Ries and Johnathon Liddicoat, 'Time to get serious about privacy policies: The special case of genetic privacy' (2014) *Federal Law* Review 42(1) 149-179. See also Health Law

short of Federal Trade Commission privacy guidelines; with few companies detailing disclosure risk or how long data would be kept.[64] Canadian research with DTCGT customers found, despite almost half reading privacy policies, most expected companies would share results only with them and destroy samples, indicating the need for more robust explanation.[65]

Concerns about privacy protection appear well placed. Research conducted in 2013 was able to re-identify selected de-identified genetic data, including DTCGT, by triangulating publicly available online databases such as voter rolls with genomic data in recreational genealogy databases, suggesting as online databases increase in size, re-identification will become easier.[66] As more individuals have genetic data and share in online communities, re-identification may have significant flow-on effects such as genetic discrimination or prejudicial treatment based on genetic status.[67] For example, Australian life, disability and income protection insurance is risk-rated and exempt from the provisions of s46 of the *Disability Discrimination Act 1992* (Cth) that prohibits discrimination based on genetic status.

Many have called for more transparency when it comes to collection, use and sharing of genetic data, including online sharing platforms.[68] In 2014, Garrison and Non went so far as to recommend DTCGT companies provide consumers with advice related to sharing and not-sharing

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Institute, University of Alberta (2010) *Analysis of Privacy Policies and Practices of Direct-to-consumer Genetic Testing Companies: Private Sector Databanks and Privacy Protection Norms*.

[64] James Hazel and Christopher Slobogin, 'Who know what, and when?: A survey of the privacy policies proferred by U.S. direct-to-consumer genetic testing companies' (2018) *Cornell Journal of Law and Public Policy, Vanderbilt Law Research Paper No 18-18.* <https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3165765>; Linnea Laestadius, Jennifer Rick and Paul Auer, 'All your data (effectively) belongs to us: data practices among direct-to-consumer genetic testing firms' (2016) *Genetics in Medicine* DOI: 10.1038/glm.2016.136.

[65] Emily Christofides and Kieran O'Doherty, 'Company disclosure and consumer perceptions of the privavy implications of direct-to-consumer genetic testing' (2016) 35(2) *New Genetics and Society* 101-123.

[66] Emiliano De Cristofaro, 'Genomic privacy and the rise of a new research community' (2014) 2 *IEEE Computer and Reliability Societies* <http://doi.ieeecomputersociety.org/10.1109/MSP.2014.24>; Melissa Gymrek, Any McGuire, David Golan, Eran Halperin and Yaniv Erlich, 'Identifying Personal Genomes by Surname Inference' (2013) 339 *Science* 321-324; Adam Tanner, 'Harvard professor re-identifies anonymous volunteers in DNA study' (2013) April *Forbes* <https://www.forbes.com/sites/adamtanner/2013/04/25/harvard-professor-re-identifies-anonymous-volunteers-in-dna-study/#76923d7192c9>.

[67] See Louise Keogh and Margaret Otlowski, 'Life insurance and genetic test results: a mutation carrier's fight to achieve full cover' (2013) 199(5) *MJA* 363-366.

[68] Tobias Haeusermann, Bastian Greshake, Alessandro Blasimme, Darja Irdam, Martin Richards and Effy Vayena, 'Open sharing of genomic data: Who does it and why?' (2017) 12(5): e01177158 *PLoS ONE* <https://doi.org/10.1371/journal.pone.0177158>; Henri-Corto Stocklé, Marie-France Mamzer-Bruneel, Guillaume Vogt and Christian Hervé, '23andMe: a new two-sided data-banking market model' (2016) 617(19) *BMC Medical Ethics* <https://bmcmedethics.biomedcentral.com/articles/10.1186/s12910-016-0101-9>.

their personal genomic information.[69] A 2017 23andMe survey found the majority of respondents were unaware of company policies, with almost one in five stating privacy concerns were their primary reason for non-purchase, which should provide a commercial incentive to enhance and publicise DTCGT privacy policies.[70]

### 4.1.3 DTCGT marketing practices

*'The powerful rhetoric used to promote these developments should be treated with caution, since it can downplay potential harms and exaggerate the usefulness of the technologies concerned.'*[71]

Since the outset, DTCGT marketing practices have been called into question.[72] In medicine, communication is designed to respect patient autonomy, providing confidential, comprehensive and objective information to both build trust and support decision-making through informed consent.[73] However, while DTCGT companies, like all commercial entities, use their online and offline marketing to inform their ultimate objective is to ultimately persuade, influencing the attitudes and purchase intentions of what are presumed to be independent and rational consumers, free to make their own marketplace choices. DTCGT consumers use marketing messages to inform, decide whether to purchase and, after purchase, use the promises made by companies to assess satisfaction, especially so for services high in credence qualities.

#### 4.1.3.1 DTCGT's marketing messages

There is an extensive body of literature analysing the marketing messages contained on DTCGT websites.[74] Indicative of the concerns raised in the literature are the risk of consumers being

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[69] Nanibaa Garrison and Amy Non, 'Direct-to-consumer genomics companies should provide guidance to their customers on (not) sharing personal genomic information' (2014) 14(11) *The American Journal of Bioethics* 55-57.

[70] Melissa Anders, 'DNA ancestry test kits are hot holiday gifts despite privacy concerns for some', 6 December 2-17, *Forbes* <https://www.forbes.com/sites/melissaanders/2017/12/06/dna-ancestry-test-kits-are-hot-holiday-gifts-despite-privacy-concerns-from-some/#32d02a613f9c>.

[71] Nuffield Council on Bioethics *Medical profiling and online medicine: the ethics of 'personalised healthcare' in a consumer age* (2010), 192. <http://nuffieldbioethics.org/wp-content/uploads/2014/07/Medical-profiling-and-online-medicine-the-ethics-of-personalised-healthcare-in-a-consumer-age-Web-version-reduced.pdf>.

[72] Media representations of DTCGT companies are beyond the scope of this research however those wanting more information should see John Lynch, Ashley Parrott, Robert Hopkin and Melanie Myers, 'Media coverage of direct-to-consumer genetic testing' (2011) 20(5) *J Genet Couns* 486-494. DOI: 10.1007/s10897-011-9374-9.

[73] See Manuel Schaper and Silke Schicktanz, 'Medicine, market and communication: ethical considerations in regard to persuasive communication in direct-to-consumer genetic testing services' (2018) 19(56) *BMC Medical Ethics* DOI: 10.1186/s12910-018-0292-3.

[74] See Amanda Singleton, Lori Erby, Kathryn Foise and Kimberly Kaphingst, 'Informed choice in direct-to-consumer genetic testing (DTCGT) websites: A content analysis of benefits, risks and limitations' (2012) 21

misled as companies tend to exaggerate and oversimplify benefits while rarely mentioning limitations or risks,[75] providing the 'illusion of scientific legitimacy',[76] with many calling for greater transparency.[77] Companies also rarely address the complexity of interpreting risk,[78] or advise of the option of foregoing DTCGT altogether or choosing CGT,[79] suggesting consent cannot be *informed* and calling to mind the caution *caveat emptor* – buyer beware. Risks such as potential emotional consequences, behavioural changes and confidentiality issues are often poorly cited on websites[80] and little scientific evidence of clinical validity is provided.[81] In 2006 and again in 2010, the US GAO investigations uncovered deceptive marketing practices such as leveraging nutrigenic test results to sell personalised supplements. These practices coupled with results variations led the GAO to conclude test results were misleading.[82]

#### *4.1.3.2 Do marketing messages matter?*

Sweeny and Legg found marketing messages influenced perceptions of benefits, expectations about regret for not testing and intention to test, with negative messaging resulting in lower

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*Journal of Genetic Counseling* 433-439; Timothy Caulfield, 'Predictive or preposterous? The marketing of DTCGT genetic testing' (2011) 10(3) *Journal of Science Communication* C02; Heidi Howard and Pascal Borry, 'Personal genome testing: Do you know what you are buying?' (2009) 9(6-7) *The American Journal of Bioethics* 11-12.

[75] See Loredana Covolo, Sara Rubinelli, G Orizio and Umberto Gelatti, 'Misuse (and abuse?) of the Concept of Empowerment. The Case of Online Offer of Predictive Direct-to-consumer Genetic Tests' (2012) 1(1) J Public Health Res 7-10; Edna Einsiedel and Rose Geransar, 'Framing genetic risk: trust and credibility markers in online direct-to-consumer advertising for genetic testing' (2009) 28(4) *New Genetics and Society* 339-362.

[76] Amy Vashlishan Murray, Michael Carson, Corey Morris and Jon Beckwith, 'Illusions of scientific legitimacy: misrepresented science in the direct-to-consumer genetic-testing marketplace' (2010) 26(11) *Trends in Genetics* 459-461.

[77] See See Norman Lewis, Debbie Treise, Stephen Hsu, William Allen and Hannah Kang, 'DTCGT genetic testing companies fail transparency prescriptions' (2011) 30(4) New Genetics and Society 291-307;elka Phillips, 'Genomic privacy and direct-to-consumer genetics" (2015) *IEEE* DOI: 10.1109/SPW.205.19.

[78] Audrey Chapman, 'DTCGT Marketing of Genetic Tests: The Perfect Storm' (2008) 8(6) *The American Journal of Bioethics* 10-11.

[79] Stephanie Bair, 'Direct-to-consumer genetic testing: Learning from the past and looking forward to the future' (2012) 67 *Food and Drug Law Journal*, 413-433.

[80] Amanda Singleton, Lori Erby, Kathryn Foisie and Kimberly Kaphingst, 'Informed choice in direct-to-consumer genetic testing (DTCGT) websites: a content analysis of benefits, risks, and limitation' (2012) 21(3) J Genet Couns 433-439. DOI: 10.1007/s10897-011-9474-6.

[81] See Norman Lewis, Debbie Treise, Stephen Hsu, William Allen and Hannah Kang, 'DTCGT genetic testing companies fail transparency prescriptions' (2011) 30(4) New Genetics and Society 291-307; Christine Lachance, L Erby, B Ford, V Allen and K Kaphingst, 'Informational content, literacy demands, and usability of websites offering health-related genetic tests directly to consumers' (2010) 12(5) Genet Med 304-312.

[82] US Government Accountability Office (2010) *Direct-to-consumer Genetic Tests: Misleading Test Results are Further Complicated by Deceptive Marketing and Other Questionable Practices* <http://www.gao.gov/products/GAO-10-847T>; US Government Accountability Office (2006) *Nutrigenetic Testing: Tests Purchased from Four Websites Mislead Customers* <http://www.gao.gov/products/GAO-06-977T>.

intentions and greater anticipated regret if tested.[83] Another study also found interest in DTCGT decreased with provision of additional risk information, with exposure to potential risk altering purchase intentions and beliefs about efficacy.[84] From a commercial perspective, studies such as these would be unlikely to encourage DTCGT companies to increase risk information provided.

### *Concerns about the DTCGT offering warranting further investigation*

Part One suggests bona fide concerns exist about test quality, contracts underlying the consumer/company relationship, and the marketing undertaken by DTCGT companies. Of particular interest is whether consumers believe DTCGT results are accurate and, after testing, feel they have sufficient information to make decisions. If they do, how do these beliefs influence, for example, their intention to gather more information or seek professional advice?

Collection and use of personal data in the online environment continues to be a concern as evidenced by its inclusion as one of the ACCC's 2019 annual priorities. Canadian research suggested even if privacy policies are read, most consumers believe their genetic data would only be shared with their permission raising the question as to whether consumers in other jurisdictions shared that belief.[85] Of particular interest is whether Australian and American beliefs were similar to their Canadian counterparts and what effect these beliefs might have on intention to share the genetic information obtained in their DTCGT results.

## PART TWO: CONCERNS ABOUT THE IMPACT ON INDIVIDUALS

Four key areas relative to individual engagement with DTCGT results have been identified in the literature as being of concern: interpretation of test results; psychological impact; behavioural impact; and sharing of genetic data and information. This part looks at the concerns discussed in the academic literature matching them with particular findings from empirical studies and meta-analysis. The empirical studies discussed in this section varied in terms of sample size and target

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[83] Kate Sweeny and Angela Legg, 'Predictors of interest in direct-to-consumer genetic testing' (2011) 26(10) *Psychology and Health* 1259-1272 (Craigslist survey of 99 members of general public).

[84] Stacy Gray, Cristin O'Grady, Lauren Karp, Daniel Smith, Sanford Schwartz, Robert Hornik and Katrina Armstrong, 'Risk information exposure and direct-to-consumer genetic testing for BRCA mutations among women with a personal or family history of breast or ovarian cancer' (2009) 18(4) *Cancer Epidemiol Biomarkers Prev* 1303-1311 (300 females shown mock DTCGT ads with positive, negative or balanced information).

[85] See, for example, Office of the Privacy Commissioner of Canada, 'A discussion paper exploring potential enhancements to consent under the *Personal Information Protection and Electronic Documents Act* (2016) <https://www.priv.gc.ca/en/opc-actions-and-decisions/research/explore-privacy-research/2016/consent_201605/>; and Health Law Institute, University of Alberta (2010) *Analysis of Privacy Policies and Practices of Direct-to-consumer Genetic Testing Companies: Private Sector Databanks and Privacy Protection Norms.*

respondents with some being one-off and others longitudinal, some presenting responses to hypothetical results and others surveying actual DTCGT consumers.[86] Several are of particular note as they represent large samples of actual DTCGT customers, allowing researchers to publish findings relative to specific aspects of DTCGT and subsets of respondents, although given their timing represent the views of early adopters. The 2009 Scripps Genomic Health Initiative (Scripps) led by Eric Topol is a longitudinal survey of 2240 consumers who purchased subsidised Navigenics DTCGT test. The 2010 Johns Hopkins study (Hopkins) led by David Kaufman is an online survey of over 1000 DTCGT customers of 23andMe, deCODEme and Navigenics. The 2012 Impact of Personal Genomics Study (PGen) funded by the NIH and led by Robert Green and Scott Roberts is a longitudinal study of over 1600 23andMe and Pathway Genomics customers.[87]

### *4.2.1 I've got my results ... what do they mean? – Interpreting DTCGT results*

*'We take complicated genetic information and distill it in language that people can actually understand.'*[88]

Anne Wojcicki, CEO 23andMe

With CGT, healthcare professionals interpret results based on their own knowledge and experience or that of experts, within the context of full medical, pharmaceutical, lifestyle and family history information of the individual – accepting responsibility and liability for this interpretation. With DTCGT, individuals interpret genetic information within their own skillset, choosing what additional information, if any, to consider, and determine their own psychological and behavioural responses. Responsibility lies solely with the individual, as noted in company disclaimers.[89]

DTCGT, like all genetic testing, is not 100% accurate even if based on the latest science and conducted in accredited laboratories. As such, the potential to generate false positive or false

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[86] Notations as to sample size and sampling are provided for selective studies to illustrate the range of studies cited.

[87] Details at <https://www.genomes2people.org/research/pgen/>. Longitudinal studies involve re-contacting initial respondents for additional data gathering.

[88] Samuel Gibbs, 'DNA-screening test 23andMe launches in UK after US ban' 2 December 2014 *The Guardian* <https://www.theguardian.com/technology/2014/dec/02/google-genetic-testing-23andme-uk-launch>. Quoting Anne Wojcicki, CEO 23andMe.

[89] See Deanna Alexis Carere, Tyler VanderWeele, Jason Vassy et al., 'Prescription medication changes following direct-to-consumer personal genomic testing: findings from the Impact of Personal Genomics (PGen) study' (2016) *Genetics in Medicine* DOI: 10.1038/gim.2016.141; Gareth Hollands, David French, Simon Griffin et al., 'The impact of communicating genetic risks of disease on risk reducing health behaviour: Systematic review with meta-analysis', (2016) *BMJ* DOI: 10.1136/bmj.i1 102.

negative results during the testing process always exists. Genetic information is extremely complex, so even with accurate test results, consumer interpretation can generate 'false positives' and 'false negatives' through over and under-estimation of disease probabilities. With bundled testing, consumers must interpret each individual result and then aggregate these interpretations into an overall risk assessment. Interpretation inconsistent with actual test results could therefore have a cumulative as well as individual effect, and, if shared with family, create a ripple effect.[90]

While companies claim results are understandable, others disagree suggesting DTCGT results yield very specific statistical information that 'may be meaningless (or at the very least difficult to understand and interpret) for an individual consumer'.[91] Shiloh et al. note bundled testing introduces additional complexity 'because conditions vary in inheritance and the availability of testing and prevention strategies'.[92] Over two-thirds of their respondents indicated they would have chosen not to receive risk information for at least one of the eight diseases tested. While not DTCGT, this illustrates an additional challenge for consumers – interpreting multiple test results, determining overall psychological and behavioural responses, and dealing with results they would rather not know. Relative to pharmacogenomic testing, Lu, Lewis and Traylor found some tests conducted by 23andMe provided useful information mirroring standard clinical tests, however others provided limited guidance suggesting value only with professional interpretation.[93]

#### *4.2.1.1 The context for DTCGT interpretation*

DTCGT is not context-neutral. In addition to personal characteristics and health status, consumers' existing health-related knowledge and attitudes provide the overarching context within which their DTCGT tests are ordered, interpreted and actioned.

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[90] The term 'inconsistent' is preferred to denote situations where interpretation does not 'match' actual results as terms such as 'accurate' or 'correct' implicitly include value judgements based on subjective criteria. These terms are however used when quoting particular research using those terms.

[91] Stephanie Bair, 'Direct-to-consumer genetic testing: Learning from the past and looking forward to the future' (2012) 67 *Food and Drug Law Journal*, 413-433, 421.

[92] Shoshana Shiloh, Christoper Wade, Scott Roberts, Sharon Hensley Alford and Barbara Biesecker, 'On averages and peaks: How do people integrate attitudes about multiple diseases to reach a decision about multiplex genetic testing" (2013) January *Medical Decision Making* 71-77, 71 (2000 individuals from the non-DTCGT Multiplex Initiative collaboration between NIH and large US healthcare system).

[93] Mengfei Lu, Cathryn Lewis and Matthew Traylor, 'Pharmacogenetic testing through the direct-to-consumer genetic testing company 23andMe' (2017) 10(47) *BMC Medical Genomics* doi.org/10.1186/s12920-017-0283-0.

### *Health-related knowledge: health literacy, genetic literacy and health numeracy*

Good health and genetic literacy, and health numeracy are important for informed healthcare decision-making and self-management of, for example, prescription drugs, particularly so in today's consumer-oriented health care environment.[94] Health and genetic literacy refer to the ability to obtain, process and understand basic health and genetic information, and health numeracy the skills needed to understand and use quantitative information.[95] International and domestic statistics suggest cause for concern, with low levels of both literacy and numeracy found in Australia and the US.[96] Illustrative of low genetic literacy is the 2018 23andMe survey finding 70% of respondents were unaware humans have 23 chromosome pairs, despite the clue in the company's name.[97]

Research suggests low health numeracy may distort risk comprehension and increase susceptibility to extraneous factors such as mood, particularly important relative to DTCGT disease predisposition tests where individuals' relative risk is generally presented in numeric form.[98] Of particular concern is research where at least a third reported lower genetic self-efficacy six months post-test, perhaps reflecting as the researchers suggest 'an appropriate re-evaluation by consumers in response to receiving complex genetic information.'[99]

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[94] See Australian Commission on Safety and Quality in Healthcare, Health Literacy: Taking action to improve safety and quality (2014), 12. National Network of Libraries of Medicine, Health Literacy <http://nnlm.gov/outreach/consumer/hlthlit.html>; Dale Lea, K Kaphingst, D Bowen, I Lipkus and D Hadley, 'Communicating Genetic and Genomic Information: Health Literacy and Numeracy Considerations' (2010) 14 *Public Health Genomics* 279-289.

[95] US Department of Health and Human Services, Office of Disease Prevention and Health Promotion, *Quick Guide to Health Literacy* <https://health.gov/communication/literacy/quickguide/factsbasic.htm>; Jessica Ancker and David Kaufman, 'Rethinking Health Numeracy: A Multidisciplinary Literature Review' (2007) 14(6) *Journal of the American Medical Informatics Association* 713-721.

[96] See OECD (2016), *The Survey of Adult Skills: Reader's Companion, Second Edition* OECD Publishing: Paris <http://dx.doi.org/10.1787/9789264258075-en>. See also Kimberly Kaphingst, Melvin Blanchard, Laurel Milam, Manusheela Pokharel, Ashley Elrick and Melody Goodman, 'Relationships Between Health Literacy and Genomics-Related Knowledge, Self-Efficacy, Perceived Importance, and Communication in a Medically Underserved Population' (2016) 21 (Suppl 1) *J Health Commun.* 58-68 (624 patients in primary care clinic); Natasha Bita, 'Literacy, numeracy skills below minimum standard', *The Australian*, January 30, 2016.

[97] 23andMe blog, 'What do you know, It's DNA Day' 25 April 2018. <https://blog.23andme/news/what-do-you-know-its-dna-day>.

[98] Valerie Reyna, Wendy Nelson, Paul Han and Nathan Dieckmann, 'How Numeracy Influences Risk Comprehension and Medical Decision Making' (2009) 135 (6) *Psychol Bull* 943-973; Australian Commission on Safety and Quality in Health Care, *Health Literacy: Taking action to improve safety and quality* (2014).

[99] Deanna Carere, Peter Kraft, Kimberly Kaphingst, Scott Roberts and Robert Green, 'Consumers report lower confidence in their genetics knowledge following direct-to-consumer personal genomic testing' (2016) 18(1) *Genetics in Medicine* 65-71, 66. Self-efficacy refers to confidence in own ability to perform. See A Bandura *Social Foundations of Thought and Action: A Social Cognitive Theory* (Prentice Hall, 1986).

*Health-related attitudes*

Health consciousness and health fatalism can be thought of as two anchors on the spectrum of health-related attitudes reflecting an active/passive stance towards health and its management. Health consciousness can be used to predict a variety of both health attitudes and behaviours as it refers to the extent individuals integrate health concerns into their daily activities.[100] Health conscious individuals accept responsibility for their health, adopt healthy lifestyles, and use active communication channels such as family discussions.[101] By contrast, health fatalism refers lack of control and powerlessness over disease, which in a genetics context presents as genetic determinism, the belief 'genes alone define biology'.[102] Fatalistic individuals are less likely to adhere to healthy lifestyle behaviours or engage in preventative measures such as disease screening.[103]

#### *4.2.1.3 How do consumers interpret DTCGT results?*

Significant research focus has been directed towards determining how actual and potential consumers understand and interpret both actual and hypothetical DTCGT test results. The Scripps study found 75% of early DTCGT customers understood their results.[104] Both the PGen and Hopkins studies found the majority of actual DTCGT consumers correctly interpreted hypothetical results, with the authors concluding respondents understood the objective nature of the risk.[105] Both identified greater comprehension in younger respondents with the PGen study also finding numeracy, genetic knowledge, and education influenced comprehension. Research by Haga et al.

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[100] See Rama Jayanti and Alvin Burns, 'The antecedents of preventive healthcare behavior: An empirical study' (1998) 26 *Academy of Marketing Science Journal* 6-15.

[101] See Frederic Kraft and Philips Goodell, 'Identifying the health conscious consumer' (1993) 13(3) *Journal of Health Care Marketing* 18-25; Mohan Dutta-Bergman, 'Primary Sources of Health Information: Comparisons in the Domain of Health Attitudes, Health Cognitions and Health Behaviours' (2004) 16(3) 273-288; Lee Kaskutas and Thomas Greenfield, 'The role of health consciousness in predicting attention to health warning messages' (1997) 11(3) *American Journal of Health Promotion* 186-193.

[102] See Niklas Gericke, Rebecca Carver, Jérémy Castéra, Nelma Evangelista, Claire Marre and Charbel El-Hani, 'Exploring Relationships Among Belief in Genetic Determinism, Genetic Knowledge, and Social Factors' (2017) 26 *Science & Education* 1223-1259.

[103] Roseanne Fairchild, 'Fatalism and Health Behaviors: Exploring the Context for Clinician-Patient Interactions' (2015) 2(4) *Annals of Nursing and Practice* 1032-1036; Jeff Niederdeppe and Andrea Levy, 'Fatalistics beliefs about cancer prevention and three prevention behaviors' (2007) 16(5) *Cancer Epidemiology, Biomarkers & Prevention* 998-1003.

[104] Cinnamon Bloss, Nathan Wineinger, Burcu Darst, Nicholas Schork and Eric Topol, 'Impact of direct-to-consumer genomic testing at long term follow-up' (2013) 50 *Journal of Medical Genetics* 393-400.

[105] Jenny Ostergren, Michele Gornick, Deanna Carere, Sarah Kalia, Wendy Uhlmann, Mack Ruffin, Joanna Mountain, Robert Green and Scott Roberts, 'How well do customers of direct-to-consumer personal genomic testing services comprehend genetic test results? Findings from the Impact of Personal Genomics Study' (2015) 18 *Public Health Genomics* 216-224; David Kaufman, Juli Bollinger, Rachel Dvoskin and Joan Scott, 'Risky Business: Risk Perception and the Use of Medical Services among Customers of DTCGT Personal Genetic Testing' (2012) 21 *Journal of Genetic Counseling* 413-422.

providing respondents with actual diabetes risk information from either a DTCGT test or provided a Board-certified genetic counsellor suggested information sources might also influence interpretation. While overall 59% correctly interpreted their risk, comprehension was significantly higher for the results provided by the trained health professional.[106]

While encouraging, if between 60-90% understood and correctly interpreted results, this means between 10-40% did not. Interpretation may also vary by disease. In the McGrath study presenting actual consumers with hypothetical results for two diseases, only one-quarter correctly interpreted both results with one-third neither.[107] And how results are presented may also impact interpretation.[108] For example, Mauboussin and Mauboussin found while most believed the word 'always' meant 100%, the probability range attributed to a 'real possibility' ranged from 20% to 80%.[109]

Research comparing general public and genetic counsellors responses to sample results found the majority of the general public found results understandable and provided correct interpretations, believing results were significantly more useful than did counsellors. However, the general public weren't able to 'accurately assess if they might benefit from assistance in understanding their DTCGT genetic test results', suggesting if individuals believe they understand results they may not seek further assistance.[110]

#### *4.2.1.4 Do test results influence risk perceptions?*

Shiloh et al. found risk perceptions relatively stable at baseline versus three months post-testing, with increased risk perceptions consistent with genetic markers found, family history and

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[106] Susanne Haga, W Barry, R Mills, L Svetkey, S Suchindran, H Willard and G Ginsburg, 'Impact of delivery models on understanding genomic risk for Type 2 Diabetes' (2014) 17 *Public Health Genomics* 95-104.
[107] Scott McGrath, Jason Coleman, Lotfollah Najjar, Ann Fruhling and Dhundy Bastola, 'Comprehension and data-sharing behaviour of direct-to-consumer genetic test customers' (2016) 19 *Public Health Genomics* 116-125.
[108] See Linda Cameron, Theresa Marteau, Paul Brown, William Klein and Kerry Sherman, 'Communication strategies for enhancing understanding of the behavioral implications of genetic and biomarker tests for disease risk: The role of coherence' (2012) 35 *J Behav Med* 286-298.
[109] Andrew Mauboussin and Michael Mauboussin, 'If you say something is 'likely' how likely do people think it is?' (2018) *Harvard Business Review* <https://hbr.org/2018/07/if-you-say-something-is-likely-how-likely-do-people-think-it-is>. See also Denise Lautenback, Kurt Christensen, Jeffrey Sparks and Robert Green, 'Communicating genetic risk information for common disorders in the era of genomic medicine' (2013) 14 *Annu. Rev. Genomics Hum. Genet.* 491-513.
[110] Justin Leighton, K Valverde and B Bernhardt, 'The general public's understanding and perception of direct-to-consumer genetic test results' (2012) 15 *Public Health Genomics* 11-21, 19 (Facebook survey of 145 general public and 171 genetic counsellors).

causality beliefs.[111] However the PGen study found significantly altered risk perceptions when comparing pre-testing to six months post-testing perceptions. The authors concluded consumers learn from their test results and update their beliefs but found medical actions were only sought in response to unexpected risks.[112] Another group of PGen researchers suggested DTCGT results alter genetic knowledge and genetic self-efficacy (confidence in own ability), with over one-third reporting lower self-efficacy six months post-test, perhaps reflecting 'an appropriate re-evaluation by consumers in response to receiving complex genetic information'.[113]

### *4.2.2 I've got my results … how do they make me feel? – Justified or unjustified affect*

Much of the empirical research has focused on assessing DTCGT's psychosocial impact and whether individuals experience adverse effects such as psychological distress post-results.[114] The majority of studies did not find evidence of psychological distress or harm resulting from receiving DTCGT results.[115] For example, Egglestone et al. noted that while one in four experienced a change in health anxiety, over 85% were reductions.[116] Scripps' researchers found no difference in anxiety levels pre/post-testing, and 3 months later, concluding there were no long-term psychological risks.[117] Gordon et al. found reasonable understanding of genomic risk information,

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[111] Shoshana Shiloh, H deHeer, S Peleg, Sharon Hensley Alford, K Skapinsky, Scott Roberts and D Hadley, 'The impact of multiplex genetic testing on disease risk perceptions' (2015) 87 *Clinical Genetics* 117-123.
[112] Joshua Krieger, Fiona Murray, Scott Roberts and Robert Green, 'The impact of personal genomics on risk perceptions and medical decision-making' (2016) 34(9) *Nature Biotechnology* 912-918, 917.
[113] Deanna Carere, Peter Kraft, Kimberly Kaphingst, Scott Roberts and Robert Green, 'Consumers report lower confidence in their genetics knowledge following direct-to-consumer personal genomic testing' (2016) 18(1) *Genetics in Medicine* 65-71, 65.
[114] The term *affect* is used to denote emotional or psychological responses.
[115] See Uta Francke, Cheri Dijamco, Amy Kiefer, Nicholas Eriksson, Bianca Moiseff, Joyce Tung and Joanna Mountain, 'Dealing with the unexpected: consumer responses to direct-access *BRCA* mutation testing' (2013) I(38) *PeerJ* DOI: 10.7717/peerj.8 (14 male and 11 female 23andMe customers receiving high-risk BRCA results); Katherine Wasson, Tonya Nashay Saunders, Nancy Hogan, Sara Cherny and Kathy Helzlsoner, 'Primary care patients' views and decisions about, experience of and reactions to direct-to-consumer genetic testing: a longitudinal study' (2013) *Journal of Community Genetics* DOI: 10.1007/s12687-013-0156-y (focus groups with 20 primary care patients who had DTCGT tests); Kimberly Kaphingst, C McBride, C Wade, S Alford, R Reid, E Larson, A Baxevanis and L Brody, 'Patients' understanding of and responses to multiplex genetic susceptibility test results' (2012) 14(7) Genet Med 681-687.
[116] Corin Egglestone, Anne Morris and Ann O'Brien, 'Effect of Direct-to-Consumer Genetic Tests on Health Behaviour and Anxiety: A Survey of Consumers and Potential Consumers' (2013) 22 *Journal of Genetic Counseling* 565-575 (online social media survey of 189 DTCGT customers and 86 potential consumers); Theresa Marteau, David French, Simon Griffin, A T Prevost, Stephen Sutton, Claire Watkinson, Sophie Attwood, and Gareth Hollands, 'Effects of communicating DNA-based disease risk estimates on risk-reducing behaviours' (2010) 10 *The Cochrane Library* 1-74 (review of 14 papers representing 7 clinical and 7 analogue studies).
[117] Cinnamon Bloss, Nathan Wineinger, Burcu Darst, Nicholas Schork and Eric Topol, 'Impact of direct-to-consumer genomic testing at long term follow-up' (2013) 50 *Journal of Medical Genetics* 393-400; Cinnamon Bloss, Laura Ornowski, Elana Silver, Michele Cargill, Vance Vanier, Nicholas Schork and Eric Topol,

the multi-factorial nature of common complex diseases and generally no negative emotional responses or overly deterministic perceptions of results.[118]

Overall, a 2018 meta-analysis of studies of DTCGT consumers found generally low levels of anxiety, worry and distress that faded with time, concluding there was 'little or no evidence for serious adverse psychological responses among consumers'.[119] In 2016, Hollands et al. found no adverse effects such as depression or anxiety in a meta-analysis of 18 trials with non-DTCGT customers.[120] These results are not surprising as the majority of DTCGTs are for low penetrance alleles with modest associated risk and limited predictive ability. Most consumers would likely receive risk estimates slightly higher or lower than population averages for most of the tests – results likely not sufficiently alarming to generate extreme psychological responses.

That being said, several empirical studies did identify higher levels of psychological distress and also noted links with individual differences in psychological composition or predispositions. For example, Scripps' researchers found 6% of DTCGT customers experienced distress responses, while over 20% of study participants were defined as being psychologically sensitive, indicating they had more pre-test concerns.[121] The Scripps study found no significant differences in baseline and follow-up anxiety, but did note greater perceived seriousness and lower perceived control over disease were associated with test related distress (anxiety).[122] They concluded greater

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'Consumer perceptions of direct-to-consumer personalized genomic risk assessments' (2010) 12(9) *Genetics in Medicine* 556-566.

[118] Erynn Gordon, Georgia Griffin, Lisa Wawak, Hauchie Pang, Sarah Gollust and Barbara Bernhardt, "It's not like judgement day": Public understanding and reactions to personalized genomic risk information' (2012) 21 *J Genet Counsel* 423-432 (60 interviewees).

[119] Kelly Stewart, Anke Wesselius, Maartje Schrerurs, Annemie Schols and Maurice Zeegers, 'Behavioural changes, sharing behaviour and psychological responses after receiving direct-to-consumer genetic test results: a systematic review and meta-analysis' (2018) 9(1) *J Community Genet* 1-18, 16 (reviewed 19 articles involving 11 studies – 7 where participants paid and 4 where they received free tests).

[120] Gareth Hollands, David French, Simon Griffin, Toby Prevost, Stephen Sutton, Sarah King and Theresa Marteau, 'The impact of communicating genetic risks of disease on risk-reducing health behaviour: systematic review with meta-analysis' (2016) 352 *BMJ* DOI: 10.1136/bmj/i1102.

[121] K Broady, K Ormond, E Topol, N Schork and Cinnamon Bloss, 'Predictors of adverse psychological experiences surrounding genome-wide profiling for disease risk' (2018) 9 *J Community Genet* 217-225.

[122] D Boeldt, N Schork, E Topol and C Bloss, 'Influence of individual differences in disease perception on consumer response to direct-to-consumer genomic testing' (2015) 87 *Clin Genet* 225-232; Cinnamon Bloss, Nathan Wineinger, Burcu Darst, Nicholas Schork and Eric Topol, 'Impact of direct-to-consumer genomic testing at long term follow-up' (2013) 50 *Journal of Medical Genetics* 393-400; Cinnamon Bloss, Nicholas Schork and Eric Topol, 'Direct-to-consumer pharmacogenomic testing is associated with increased physician ultilisation' (2014) 51 *Journal of Medical Genetics* 83-89.

perceived control might protect against adverse outcomes while higher perceived seriousness might make individuals more psychologically sensitive.[123]

While not DTCGT, the Risk Evaluation & Education for Alzheimer's Disease study (REVEAL) provides some insight as to predictors of distress. Although younger age was found to be a predictor of psychological sensitivity and family history for Alzheimer's a predictor for distress, the difficulty in identifying psychological sensitivity pre-test was noted. REVEAL researchers found worry was more closely related to likelihood perceptions (lifetime chance of developing condition) than severity perceptions (impact of having disease).[124] Research also found asymptomatic children of Alzheimer's patients with higher emotional distress pre-test were more likely to have emotional difficulties post-test.[125]

While the empirical research would suggest *most* consumers do not experience significant psychological distress, *some* do.[126] However, rather than measuring absolute levels of psychological distress, what needs to be determined is whether psychological distress is justified or unjustified given actual test results and consumer interpretation of these results. For example, while 40% of respondents in the Bansback study anticipated being more worried in response to hypothetical results, this was associated with higher levels of disease risk, representing justified affect.[127]

More challenging to determine is if psychological distress experienced is based psychological disposition rather than interpretation. As noted, this is difficult to determine pre-test, and may not be known post-test if individuals do not disclose. For example, psychological distress may

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[123] D Boeldt, N Schork, E Topol and C Bloss, 'Influence of individual differences in disease perception on consumer response to direct-to-consumer genomic testing' (2015) 87 *Clin Genet* 225-232.
[124] Shoshana Shiloh, Christopher Wade, Scott Roberts, Sharon Hensley Alford and Barbara Biesecker, 'Associations between risk perceptions and worry about common diseases: A between- and within subject examination' (2013) 28(4) *Psychology and Health* 434-449 (non-DTCGT Risk Evaluation & Education for Alzheimer's Disease (REVEAL).
[125] Robert Green, Scott Roberts, Adrienne Cupples, Norman Relkin, Peter Whitehouse, Tamsen Brown, Susan LaRusse Eckert, Melissa Butson, Dessa Sadovnick, Kimberly Quaid, Clara Chen, Robert Cook-Deegan and Lindsay Farrer, 'Disclosure of *APOE* genotype risk for Alzheimer's' (2009) 36(13) *New England Journal of Medicine* 245-254.
[126] See Suzanne O'Neill, Kenneth Tercyak, Chanza Baytop, Sharon Alford and Colleen McBride, 'A new approach to assessing affect and emotional implications of personal genomic testing for common disease risk' (2015) 18 *Public Health Genomics* 104-112 (228 adults).
[127] Nick Bansback, Sonia Sizto, Daphne Guh and Aslam Anis, 'The Effect of Direct-to-Consumer Genetic Tests on Anticipated Affect and Health-Seeking Behaviors: A Pilot Survey' (2012) 16(10) *Genetic Testing and Molecular Biomarkers* 1165-1171 (370 members of the Canadian general public recruited through online market research panel).

occur even if risk is low[128] or 'simply through people worrying excessively or becoming neurotic over … small increases in risk'.[129] Lippi et al. go so far as to suggest 'false reassurance' arising from 'false negative' results …might be as deleterious as the 'unjustified anxiety' secondary to the 'false positive results'.[130]

### 4.2.3 *I've got my results …now what do I do? – Appropriate and sustained or inappropriate behaviour*

*'For any genetic tests, you have to understand what you are going to do with results – positive, negative or uncertain – and what impact that result may have on you and your family.'*[131]

DTCGT's promise of consumer empowerment is provided by access to personal genetic information. Its true value comes from consumers using that information in autonomous, informed healthcare decisions and implementing sustainable lifestyle changes, 'making appropriate behavioural changes in response to increased risk'.[132] However, there is also potential for harm if inappropriate behavioural responses are undertaken, say, not seeking preventative measures such as vigilant screening in response to increased risk.

#### 4.2.3.1 *Appropriate health behaviours and intentions*

Healthcare professionals routinely dispense the same basic risk-reducing lifestyle advice for a range of diseases and symptoms: eat less and better, move more, drink in moderation, don't smoke or consume drugs, and use sunscreen – all behaviours within individuals' control, all communicated extensively in the media. Yet health statistics on obesity and Type 2 Diabetes for example, would indicate this professional advice is not being actioned by significant numbers. So,

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[128] Thierry Frebourg 'Direct-to-consumer genetic testing services: what are the medical benefits?' (2012) 20 *European Journal of Human Genetics* DOI: 10.1038/ejhg.2011.229. See also Serena Oliveri, Chiara Renzi, Marianna Masiero and Gabriella Pravettoni, 'Living at risk factors that affect the experience of direct-to-consumer genetic testing' (2015) 90(10) *Mayo Clin Proc* 1323-1326.

[129] Alison Lashwood, 'The 23andMe experience – a lot of knowledge of little help?' (2015) 23 February *Bionews*, <https://www.geneticsandsociety.org/article/23andme-experience-lot-knowledge-little-help>. Quoting Dr Ewan Birney, Associate Director, European Bioinformatics Institute, Cambridge UK; Serena Oliveri and Gabriella Pravettoni, 'The disclosure of direct-to-consumer genetic testing: Sounding out the psychological perspective of consumers' (2016) 8(5) *Bio Med* DOI: 10.4172/0974-8369.100316.

[130] Giuseppe Lippi, Emmanuel Favaloro and Mario Plebani, 'Direct-to-consumer testing: more risks than opportunities' (2011) 65(12) *International Journal of Clinical Practice* 1221-1229.

[131] M Barton, 'Health behaviours not significantly changed by direct-to-consumer genetic testing' (2017) 67(3) *CA Cancer J Clin* 175-176, 176. Quoting genetics counsellor Nancy Cohen.

[132] Timothy Caulfield, 'The direct-to-consumer genetic testing fog' (2017) <http://policyoptions.irpp.org/magazines/may-2017/the-direct-to-consumer-genetic-testing-fog-column-by-timothy-caulfield/>; Erynn Gordon, Georgia Griffin, Lisa Wawak, Hauchie Pang, Sarah Gollust and Barbara Bernhardt, "It's not like judgement day": Public understanding and reactions to personalized genomic risk information' (2012) 21 *J Genet Counsel* 423-432, 423.

would adding genetic risk information into the mix make a difference? Would consumers armed with their own genetic information be empowered to make appropriate and sustained behavioural change – when basic professional advice has failed?[133]

Research has focused on measuring actual or self-reported behavioural change with early DTCGT consumers and behavioural intention with potential consumers responding to hypothetical results. Behavioural intention is often used as a measure of motivation and while it does not guarantee behaviour, it does precede behaviour, providing insight into likelihood of future behaviours.[134] The Theory of Planned Behaviour (TBT) suggests the greater the intention; the more likely the behaviour will be adopted.[135] While there is not a causal relationship between intention and behaviour as variables can intervene, intention does precede behaviour. Behaviours are influenced by the belief that expected outcomes will occur if behaviours are adopted, and subjective evaluations of associated benefits and risks. Individuals determine if current behaviour is putting them at risk, if changing would reduce risk, and finally their own ability to change, including skills, time and money.[136] From a health-related perspective, individuals' perceived controllability of health circumstances influences intention to engage in precautionary or preventative behaviour and the greater the intention, the greater the likelihood of actual behavioural change.[137]

Converting behavioural intention into sustained behavioural change is not easy as anyone who has attempted to diet or quit smoking can attest. Relative to genetic testing, Marteau and Lerman suggest that 'Just telling people they are at risk of developing a disease is rarely sufficient to

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[133] See Colleen McBride, Laura Koehly, Saskia Sanderson and Kimberly Kaphingst, 'The behavioral response to personalized genetic information: Will genetic risk profiles motivate individuals and families to choose more healthful behaviours? (2010) 31 *Annu. Rev. Public Health* 89-103; Nora Henrikson, Deborah Bowen and Wylie Burke, 'Does genomic risk information motivate people to change their behavior?' (2009) 1(37) *Genome Medicine* DOI: 10.1186.gm37.

[134] See Theresa Marteau and Caryn Lerman, 'Genetic risk and behavioural change' (2001) 322 *BMJ* 1056-1059.

[135] See Icek Ajzen, 'The Theory of Planned Behaviour' (1991) 50 *Organisational Behavior and Human Decision Processes* 179-211.

[136] See Ruth Jepson, Fiona Harris, Stephen Platt and Carol Tannahill, 'The effectiveness of interventions to change six health-behaviours: A review of reviews' (2010) 10(538) *BMC Public Health* <http://www.biomedcentral.com/1471-2458/10/538>; Richard Ryan, Heather Patrick, Edward Deci and Geoffrey Willians, 'Facilitating health behaviour change and its maintenance: interventions based on self-determination theory' (2008) 10 *The European Health Psychologist* 2-5; Gerko Kok, Bart can den Borne and Patricia Colan Mullen, 'Effectiveness of health education and health promotion: meta-analyses of effect studies and determinants of effectiveness' (1997) 30(1) *Patient Education and Counseling* 19-27.

[137] See Christopher Armitage and Mark Connor, 'Efficacy of the theory of planned behaviour: A meta-analytic review' (2001) 40 *British Journal of Social Psychology* 471-499; Gaston Godin and Gerjo Kok, 'The theory of planned behaviour: A review of its applications to health-related behaviours' (1996) 11(2) *Am J Health Promot* 87-98.

change behaviour' as motivation to change is based on pre-existing perceptions such as fatalistic beliefs and whether results are accompanied by access to evidence-based interventions.[138] For example, high risk results coupled with fatalistic beliefs may actually result in decreased motivation as individuals question perceived efficacy of behavioural change – a case of 'why bother, can't fight genetics'. Subsequent research concluded behavioural change patterns in DTCGT were consistent with broader trends evidenced in genetic testing.[139]

Indicative of DTCGT studies, Egglestone et al, Nielsen et al. and Kaufman et al. all found approximately one-third of respondents reported positive diet and exercise changes, although for the Hopkins study intention was much higher than actual exercise change.[140] However, PGen researchers found those with elevated cancer risk were not significantly more likely to change diet, exercise or advanced care planning, compared to individuals with average or reduced risk six months post-testing.[141] Bansback et al. reported 57% intended to make lifestyle change but Marteau's research found only a small effect on self-reported diet and intention to change behaviour with little or no effect on smoking and physical activity.[142] Scripps' researchers also found no significant behavioural changes at baseline or follow-up, concluding that there is 'little evidence that mere provision of genetic information alone results in widespread changes in lifestyle health behaviours'.[143]

Relative to individual non-DTCGT studies, while most participants in Gordon's research expressed intention to use results to improve health, one-third actually did. Those reporting no change

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[138] Theresa Marteau and Caryn Lerman, 'Genetic risk and behavioural change' (2001) 322 *BMJ* 1056-1059, 1057.

[139] See Theresa Marteau, David French, Simon Griffin, A T Prevost, Stephen Sutton, Claire Watkinson, Sophie Attwood, and Gareth Hollands, 'Effects of communicating DNA-based disease risk estimates on risk-reducing behaviours' (2010) 10 *The Cochrane Library* 1-74.

[140] Daiva Nielsen, Deanna Carere, Cathering Wang, Scott Roberts and Robert Green, 'Diet and exercise changes following direct-to-consumer personal genomic testing' (2017) 10(24) *BMC Medical Genomics* DOI: 10.1186/s12920-017-0258-1; Corin Egglestone, Anne Morris and Ann O'Brien, 'Effect of Direct-to-Consumer Genetic Tests on Health Behaviour and Anxiety: A Survey of Consumers and Potential Consumers' (2013) 22 *Journal of Genetic Counseling* 565-575.

[141] Stacy Gray, Sarah Gollust, Deanna Carere, Clara Chen, Angel Cronin, Sarah Kalia, Huma Rana, Mack Ruffin, Catherine Wang, Scott Roberts and Robert Green, 'Personal genomic testing for cancer risk: Results from the Impact of Personal Genomics study' (2017) 35(6) *Journal of Clinical Oncology* 636-644.

[142] Nick Bansback, Sonia Sizto, Daphne Guh and Aslam Anis, 'The Effect of Direct-to-Consumer Genetic Tests on Anticipated Affect and Health-Seeking Behaviors: A Pilot Survey' (2012) 16(10) *Genetic Testing and Molecular Biomarkers* 1165-1171; Theresa Marteau, David French, Simon Griffin, A T Prevost, Stephen Sutton, Claire Watkinson, Sophie Attwood, and Gareth Hollands, 'Effects of communicating DNA-based disease risk estimates on risk-reducing behaviours' (2010) 10 *The Cochrane Library* 1-74.

[143] Cinammon Bloss, Lisa Madlensky, Nicholas Schork and Eric Topol, 'Genomic information as a behavioural health intervention: Can it work?' (2011) 8(6) *Per Med* 659-667, 659; Cinnamon Bloss, Nicholas Schork and Eric Topol, 'Effect of Direct-to-Consumer Genomewide Profiling to Assess Disease Risk' (2011) 364(6) *New England Journal of Medicine* 524-534.

believed they were already practicing good health behaviours, didn't consider themselves at risk or weren't surprised by the results.[144] While Stewart's meta-analysis found 23% engaged in positive lifestyle change with 12% improving diet and exercise regimes and 19% quitting smoking,[145] Hollands' meta-analysis of non-DTCGT studies revealed no significant effects on proactive health change or motivation to change.[146] While the positive benefits of knowing one's DNA on health behaviours is touted by the industry, the evidence does not suggest substantive positive behavioural change.

#### *4.2.3.2 Inappropriate behaviours and intentions*

Of particular concern in the DTCGT space is *inconsistent interpretation* and *unjustified* affect from under or over-estimation of risk resulting in *inappropriate* behaviour – for example, under-estimation deterring individuals from taking preventative measures or seeking medical attention where genuinely warranted, with over-estimation prompting unnecessary medical interventions.[147] It must be noted that quantifying either of these outcomes is problematic e.g. quantifying non-behaviour when warranted.

Regulators have also expressed concerns about inappropriate behavioural responses as illustrated in the FDA's 2013 communication with 23andMe: '… if the BRCA-related risk assessment for breast or ovarian cancer reports a false positive, it could lead a patient to undergo prophylactic surgery, chemoprevention, intensive screening, or other morbidity-inducing actions, while a false negative could result in a failure to recognize an actual risk that may exist.'[148] That being said, in Australia medical and pharmaceutical interventions are only available within the gatekeepered

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[144] Erynn Gordon, Georgia Griffin, Lisa Wawak, Hauchie Pang, Sarah Gollust and Barbara Bernhardt, "It's not like judgement day": Public understanding and reactions to personalized genomic risk information' (2012) 21 *J Genet Counsel* 423-432.

[145] Kelly Stewart, Anke Wesselius, Maartje Schrerurs, Annemie Schols and Maurice Zeegers, 'Behavioural changes, sharing behaviour and psychological responses after receiving direct-to-consumer genetic test results: a systematic review and meta-analysis' (2018) 9(1) *J Community Genet* 1-18 (11 studies, 7 paid and 4 free tests).

[146] Gareth Hollands, David French, Simon Griffin, Toby Prevost, Stephen Sutton, Sarah King and Theresa Marteau, 'The impact of communicating genetic risks of disease on risk-reducing health behaviour: systematic review with meta-analysis' (2016) 352 *BMJ* DOI: 10.1136/bmj/i1102.

[147] See G Samuel, C Jordens and I Kerridge, 'Direct to consumer personal genome testing: ethical and regulatory issues that arise from wanting to 'know' your DNA' (2010) 40 *Internal Medicine Journal,* 220-224, 221-22; David Hunter, Muin Khoury and Jeffrey Drazen, 'Letting the genome out of the bottle − Will we get our wish? (2008) 358(2) *New England Journal of Medicine* 105-107.

[148] Alberto Gutierrez, US Food and Drug Administration. Inspections, compliance, enforcement, and criminal investigations. Document number: GEN1300666 (2013) 22 November. 11/22/13 <https://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm376296.htm>.

medical sphere so interventions are not within the individual's control other than seeking assistance.[149]

Some behaviour is well within an individual's control such as medication regimes. PGen researchers found, while almost 6% changed or started medication based on their DTCGT results, more than 80% did so after seeking expert opinion with under 1% making independent changes.[150] The Hopkins study found 10% had changed at least one supplement but less than 5% had changed medication, with less than 1% without expert advice.[151] Of significant concern is that 1% who independently change their medication regimes as such changes can have potentially significant outcomes.

### *4.2.4 I've got my results …who do I tell? – Sharing with family, online and DTCGT companies*

Individuals who share DTCGT results, by their actions, 'breach' their own privacy, with minimal if any assurance information will not be further shared.

#### *4.2.5.1 Sharing with family*

The familial nature of genetic information means DTCGT results affect more than just the individual tested. Sharing test results may prompt increased concern and vigilance from family members – or at least prompt discussion and provide insight into family history. For example, in one small study, BRCA-positive DTCGT results prompted testing of previously unconcerned relatives. Almost half tested positive, receiving 'potentially life-saving information they might not have obtained otherwise'.[152] However, inconsistent interpretation, unjustified affect, and inappropriate behavioural responses may also be shared, creating a ripple effect as noted earlier. While the industry argues individuals have the 'right to know', commentators have suggested this

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[149] Barring medical tourism where individuals go offshore for cheaper or unavailable interventions, or unethical or negligent healthcare professionals.

[150] Deanna Carere, Tyler VanderWeele, Jason Vassy, Cathelijne van der Wouden, Scott Roberts, Peter Kraft and Robert Green, 'Prescription medication changes following direct-to-consumer personal genomic testing: Findings from the Impact of Personal Genomics (PGen) study' (2017) 19(5) *Genetics in Medicine* 537-545.

[151] David Kaufman, Juli Bollinger, Rachel Dvoskin and Joan Scott, 'Risky Business: Risk Perception and the Use of Medical Services among Customers of DTCGT Personal Genetic Testing' (2012) 21 *Journal of Genetic Counseling* 413-422.

[152] Uta Francke, Cheri Dijamco, Amy Kiefer, Nicholas Eriksson, Bianca Moiseff, Joyce Tung and Joanna Mountain, 'Dealing with the unexpected: consumer responses to direct-access *BRCA* mutation testing' (2013) I(38) *PeerJ* DOI: 10.7717/peerj.8.

right should be companioned with the 'right to not know'.[153] This latter right refers to giving potentially impacted family members the choice as to whether to receive DTCGT information and tested individuals' incidental findings from subsequent research.[154]

#### *4.2.5.2 Sharing online*

Traditionally healthcare providers have been the primary source of health-related information. However, the Internet is increasingly being used as a substantive information source and for self-diagnosis, both complementing and replacing healthcare providers, changing how medical decisions are made.[155] According to the Australian government, 78% of adults use the Internet to find health-related information.[156] Trust in all information sources is crucial, as the more individuals trust sources, the more likely they are to believe and potentially action provided information.[157] As such trust in sources such as doctors and the Internet might dictate which source is turned to for sharing and advice.

Concern has been raised about the psychological impact of excessive searching (termed cyberchondria)[158] and the accuracy of information provided, ranging from scientifically and medically substantiated to unverified and unverifiable conjecture.[159] Of particular concern are online symptom trackers used for self-diagnosis considering that in 2013, only half of those

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[153] See Benjamin Berkman and Sara Chandros Hull, 'The 'right to not know' in the genomic era: Time to break from tradition?' (2014) 14(3) *Am J Bioeth.* 28-31.
[154] See Ronni Sandroff, 'Direct-to-Consumer Genetic Tests and the Right to Know' (2010) 40(5) *The Hastings Center Report* 24-25. See also UNESCO *Universal Declaration on the Human Genome and Human Rights* (1997) Art 5 and Council of Europe, *Bioethics Convention on Human Rights and Biomedicine* (1997) Art 10.
[155] See Kofi Osei-Frimpong, Alan Wilson and Fred Lemke, 'Patient co-creation activities in healthcare service delivery at the micro level: The influence of online access to healthcare information' (2018) 126 *Technological Forecasting and Social Change* 14-27; Yen-Yuan Chen, Chia-Ming Li, Jyh-Chong Liang and Chin-Chung Tsai, 'Health information obtained from the Internet and changes in medical decision making: Questionnaire development and cross-sectional survey' (2018) 20(2) *Journal of Medical Internet Research* DOI:10.2196/jmir.9370.
[156] Australian Institute of Health and Welfare, *Australia's Health 2018: In brief* (2018) Cat. no AUS222: Canberra, AIHW, 49.
[157] See Laura Sbaffi and Jennifer Rowley, 'Trust and credibility in web-based health information: A review and agenda for future research' (2017) 19(6) *Journal of Medical Internet Research* DOI:10.2196/jmir.7579; Diane Smith, 'Health care consumer's use and trust of health information sources' (2011) 4(3) *Journal of Communication in Healthcare* 200-210; Rob Lawson, Sarah Forbes and John Williams, 'Patterns of trust in sources of health information, (2011) 124(1328) *The New Zealand Medical Journal* <https://nzma.org.nz/journal>.
[158] Emily Doherty-Torstrick, Kate Walton and Brian Fallon, 'Cyberchondria: Parsing health anxiety from online behaviour' (2016) 57(4) *Psychosomatics* 390-400.
[159] Yeolib Kim, 'Trust in health information websites: A systematic literature review on the antecedents of trust' (2016) 22(2) *Health Informatics Journal* 355-369; Wan-Ying Lin, Xinzhi Zhang, Hayeon Song and Kikuro Omori, 'Health information seeking in the Web 2.0 age: Trust in social media, uncertainty reduction, and self-disclosure' (2016) 56 *Computers in Human Behaviour* 289-294.

consulting doctors after online self-diagnosis had findings confirmed.[160] Online interpretation sites are also increasingly being used to gain risk information for diseases not covered in DTCGT test results, a process often facilitated by larger DTCGT companies who allow direct uploading of raw data files.[161]

Individuals also go online to share health information on social media, blogs and online health communities. These communities connect geographically dispersed groups of potentially anonymous users, 'fundamentally changing the way individuals manage their healthcare and chronic conditions'.[162] Members are provided with psychosocial support and opportunities to share personal experiences and resources.[163] Information quality, system infrastructure and security vary, opening the potential for hacking, misuse of personal information shared, and its use in targeted marketing.[164] While membership is free, continued site usage is governed by terms and conditions and privacy policies, with many clearly stating their intention to monetise information, again with data being used as currency.[165]

Member participation is strongly encouraged, as health-related information is a 'byproduct of the communication activity of the community'.[166] Research conducted by Lee et al. found almost half of DTCGT customers sharing results on social media, almost three-quarters went online for

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[160] See Hannah Semigran, David Levine, Shantanu Nundy and Ateev Mehrotra 'Comparison of physician and computer diagnostic accuracy' (2016) 176(12) *JAMA Internal Medicine* 1860-1861; Pew Research Center, *Health Online 2013* (2013) <http://pewinternet.org/Reports/2013/Health-online.aspx>.

[161] See Lauren Badalato, Louisa Kalokairinou and Pascal Borry, 'Third party interpretation of raw genetic data: an ethical exploration' (2017) 25 *European Journal of Human Genetics* 1189-1194.

[162] Allen Johnston, James Worrell, Paul Di Gangi and Molly Wasko, 'Online health communities: An assessment of the influence of participation on patient empowerment outcomes' (2013) 26(2) *Information Technology & People* 213-235, 214. See also Chinmoy Nath, Jina Huh, Abhishek Adupa and Siddhartha Jonnalagadda, 'Website sharing in online health communities: A descriptive analysis' (2016) 18(1) *Journal of Medical Internet Research* DOI: 10.2196/jmir.5237.

[163] See Paul Wicks, Michael Massagli, Jeana Frost, Catherine Brownstein, Sally Okun, Timothy Vaughan, Rickard Bradley and James Heywood, 'Sharing health data for better outcomes on Patients Like Me' (2010) 12(2) *Journal of Medical Internet Research* DOI:10.2196/jmir.1549.

[164] See 'Sharing reliable health information', NIH News in Health, April 2015 newsletter <https://newsinhealth.nih.gov/issue/apr2015/feature1>; Lauren Solberg, 'The benefits of online health communities' (2014) 16(4) *Virtual Mentor, AMA Journal of Ethics* 270-274; Vassilis Ragoussis, Idal Feze and Yann Joly, 'Sharing genetic information online: An exploration of GINA's 2.0 frontier' (2014) 14(11) *The American Journal of Bioethics* 53-55.

[165] See Paul Wicks, Michael Massagli, Jeana Frost, Catherine Brownstein, Sally Okun, Timothy Vaughan, Rickard Bradley and James Heywood, 'Sharing health data for better outcomes on Patients Like Me' (2010) 12(2) *Journal of Medical Internet Research* DOI:10.2196/jmir.1549.

[166] Allen Johnston, James Worrell, Paul Di Gangi and Molly Wasko, 'Online health communities: An assessment of the influence of participation on patient empowerment outcomes' (2013) 26(2) *Information Technology & People* 213-235, 215. See also Nicole Dalmer, 'Questioning relability assessments of health information on social media' (2017) 105 (1) *Journal of the Medical Library Association* DOI: dx.doi.org/10.5195/jmla.2017.108.

interpretation assistance and over half either downloaded raw data or emailed results to others.[167] Resnik suggests individuals sharing on social networks may not fully understand potential consequences and they are not just risking their own confidentiality but that of family members.[168] They may also not realise data usage, monetisation and privacy are dictated by each of these 'free' site's Terms of Service and Privacy Policies including disclaimers.

#### *4.2.5.3 Sharing with DTCGT companies*

*'The long game here is not to make money selling kits, although the kits are essential to get the base level data. Once you have the data, (the company) does actually become the Google of personalised health care.'*[169]

The opportunity to aggregate DTCGT-generated genetic data with self-report phenotype and medical data from loyal, willing, interested and re-contactable customer cohorts has led to new forms of 'participant-led research methodologies'– so called 'genetic crowdsourcing'.[170] Accessing large sample sizes necessary but difficult to obtain in traditional genetic clinical trials at significantly lower cost provides '… an important and complementary nexus of discovery to traditional academic and public health research laboratories',[171] leading to 'more rapid advancement of knowledge'.[172] Re-contactable cohorts ensure data is kept alive and growing as every additional survey question asked generates millions of new data points – all at the click of a mouse. And links to wearable fitness trackers such as Fitbits and online tools such as Apple's Research Kit ensure continuous data provision.

Genetic data from DTCGT results, raw data files, and individuals' volunteered information from online platforms can be aggregated into extremely valuable databases, ripe for monetisation,

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[167] Sandra Soo-Jin Lee, Simone Vernex, K Ormond and Mark Granovetter, 'Attitudes towards social networking and sharing behaviours among consumers of direct-to-consumer personal genomics' (2013) 3 *J Pers. Med.* 275-287.
[168] David Resnik, 'Direct-to-consumer genomics, social networking and confidentiality' (2009) 9(6-7) *Am J Bioeth* 45-46.
[169] Sarah Zhang, 'Big pharma would like your DNA' (2018 27 July *The Atlantic* <https://www.theatlantic.com/science/archive/2018/07/big-pharma-dna/566240/>. Quoting an unnamed 23andMe board member.
[170] Anna Harris, Sally Wyatt and Susan Kelly, 'The gift of spit (and the obligation to return it)' (2013) 16(2) *Information, Communication & Society* 236-257, 236.
[171] Melanie Swan, 'Multigenic condition risk assessment in direct-to-consumer genomic services' (2010) 12(5) *Genetics in Medicine* 279-288, 286.
[172] Sancy Leachman, Daniel MacArthur, Misha Angrist, Stacy Gray, Angela Bradbury and Daniel Vorhaus, 'Direct-to-Consumer Genetic Testing: Personalized Medicine in Evolution' (2011) *Genomics Law Report* 34-40, 39.

creating, in essence, privately controlled biobanks.[173] Contractual terms including no benefit sharing and waivers of property rights (if ultimately needed) ensure data can be monetised, creating a hybridisation of research and commercial activities. This makes it difficult to distinguish knowledge-seeking from profit-seeking endeavours − with the consumer actually paying to be part of the process.[174] Harris, Wyatt and Kelly found research portrayed as a form of gift exchange, using social ties to create loyal re-contactable cohorts, while drawing attention away from the 'free, clinical labour' driving corporate profitability.[175] In terms of specific marketing themes, Saukko noted early DTCGT framing of *genes as information* changed to the current *genes as data* − an abundant resource to be browsed, correlated and shared. Not only has this changed genes' social and economic meaning, it has legitimised business models that combine consumer genetics with private biobanking.[176]

Changing the lens from DNA as the 'essence of YOU' to DNA as a powerful storage device and its content as code provides companies with a data resource − one they can write, copy, edit and print at will. DTCGTs who choose to monetise operate use a simple equation: more tests bundled together = more attractive value proposition to consumers and more sales = more spit provided = larger databases = more data to mine, publish and sell = research legitimacy and profit. DTCGT tests kits are clearly being employed as 'loss leaders' – a marketing tactic offering one product at low cost to encourage patronage.[177]

Illustrative of this is 23andMe, whose business model is clearly designed to encourage consumer participation, providing a useful illustration of the value of big data, both in research and monetisation.[178] Tutton and Prainsack argue the 23andMe model promoted 'the idea that curiosity about one's genome on the one hand, and participation in research on the other, are not

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[173] Angela Mulholland, 'Privacy concerns after 23andMe shares genetic data with major drugmaker' 27 July 2018 *CTVnews.ca* <https://www.ctvnews.ca/health/privacy-concerns-after-23andme-shares-genetic-data-with-major-drugmaker-1.4030480>; Deborah Peel, 'The hidden dangers of do-it-yourself genetic tests' 16 December 2017 *Newsweek* <https://www.newsweek.com/hidden-danger-do-it-yourself-genetic-tests-749475>; Kayte Spector-Bagdady, 'The Google of healthcare: enabling the privatization of genetic bio/databanking' (2016) 26 *Annals of Epidemiology* 515-519.

[174] See Laura DeFrancesco, '23andMe's designer baby patent' (2014) 32(1) *Nature Biotechnology* 8; Lisa Miller 'The Google of Spit' (2014) 22 April <http:www.nymag.com/news/features/23andme-2-14-4/#print>.

[175] Anna Harris, Sally Wyatt and Susan Kelly, 'The gift of spit (and the obligation to return it)' (2013) 16(2) *Information, Communication & Society* 236-257, 236.

[176] Paula Saukko, 'Shifting metaphors in direct-to-consumer genetic testing" from genes as information to genes as big data' (2017) 36(3) *New Genetics and Society* 296-313.

[177] See Henir-Corto Stoeklé, Marie-France Mamzer-Bruneel, Guillaume Vogt and Christian Hervé, '23andMe: a new two-sided data-banking market model' (2016) *BMC Medical Ethics* DOI: 10.1186/s12910-016-0101-9.

[178] Cinnamon Bloss, Burcu Darst, Eric Topol and Nicholas Schork, 'Direct-to-consumer personalized genomic testing' (2011) 20(2) *Human Molecular Genetics* R132-R141, R138.

only compatible but complementary aspects of being an entrepreneurial subject of contemporary health and medicine framed by the technologies of web 2.0.'[179] Consent is obtained at the testing stage, before individuals receive results, at their highest level of interest, anticipation and motivation. Approximately 80% of customers consent to allow their genetic data to be used in company research, with the average customer contributing to over 230 studies.[180]

Given a reported five million+ customer base, the gallons of spit 'donated' represent an immense pool of mineable data, allowing for the company's own research and collaborations with government, academic and medical researchers.[181] For example, 23andMe conducted the largest-ever case-controlled GWAS for Parkinson's, ultimately identifying new genes influencing susceptibility.[182] However, the company's foray into the traditional medical research space has not been without controversy. For example, publication of its first peer-reviewed study was delayed for six months as journal editors debated the company's ethics, consent, and data-sharing procedures.[183]

But more significantly, DTCGT's extensive databases are extremely valuable to the corporate research sector, particularly pharmaceutical companies. Research in this sector is extremely expensive and time-consuming, with the average drug costing between $US4-11 billion and taking 11-14 years for the 10% that make it through clinical trials and government approvals to pharmacy shelves.[184] The appeal of DTCGT databases is obvious in terms of cost and time as evidenced by GlaxoSmithKline's investment of $US300 million in 23andMe in 2018 for four years exclusive rights to use their database for drug development.[185]

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[179] Richard Tutton and Barbara Prainsack, 'Enterprising or altruistic selves? Making up research subjects in genetic research' (2011) 33(7) *Sociology of Health & Illness* 1081-1095, 1081.
[180] Sarah Zhang, '23andMe wants its DNA database to be less white' (2018) 23 April *The Atlantic* <https://www.theatlantic.com/science/archive/2018/04/23andme-diversity-dna/558575/>.
[181] See <https://www.23andme.com/publications/for-scientists/> and 23andMe Press Release '23andMe scientists receive approximately $1.4 million in funding from the National Institutes of Health' 29 June 2014 <http//:mediacenter.23andMe.com/press-releases/nih_grant_2014>.
[182] Chuong Do, Joyce Tung, Elizabeth Dorfman, Amy Kiefer, Emily Drabant, Uta Francke, Joanna Mountain, Samuel Goldman, Caroline Tanner, Willian Langston, Anne Wojcicki and Nicholas Eriksson, 'Web-based genome-wide association study identified two novel loci and a substantial genetic component for Parkinson's Disease' (2011) 7(6) *PLoS Genetics* DOI:10.1371/journal.pgen.1002141.
[183] See Greg Gibson and Gregory Copenhaver, 'Consent and Internet-enabled human genomics' 2010 6(6) *PLoS Genetics* <https://doi.org.1371/journal.pgen.1000993>.
[184] Matthew Herper, 'The truly staggering cost of inventing new drugs' 10 February 2012 *Forbes.com* <https://www.forbes.com/sites/matthewherper/2012/02/10/the-truly-staggering-cost-of-inventing-new-drugs/#28d4e1b64a94>.
[185] Anon 'GSK and 23andMe sign agreement to leverage genetic insights for the development of novel medicines' 25 July 2018 <https://www.gsk.com/en-gb/media/press-releases/gsk-and-23andme-sign-agreement-to-leverage-genetic-insights-for-the-development-of-novel-medicines/>.

Concern has been raised that DTCGT research is 'blurring the line between consumer and research subjects' with consumers potentially unaware despite relative corporate transparency.[186] It has been suggested 'consumers who become research participants should be treated with the same respect and under the same norms as those involved in biobank research'.[187] While participation in medical and biobank research is only by informed consent, participation in company research is governed by contractual agreements. For example, key sections in 23andMe's Privacy Policy concerning data sharing and Consent for research participation indicate individuals consent to their genetic and de-identified personal data being used in scientific publications, government funded research, and research conducted with, or on behalf of, third parties such as pharmaceutical companies and commonly owned entities.[188] Use of individual-level or aggregate genetic information and self-reported information in individual research projects does not require specific consent, with research usage clearly stated as open-ended. Additional consent is obtained only for specific studies where contact with identified consumers is required. While consumers can opt-out after consenting, overall DTCGT consent is *non-specific* and *enduring* – rather than the *specific, non-enduring* informed consent typical in medical research, where oft out after consent is also available.[189] Some have even questioned whether the concept of informed consent is suitable to genetics research since the greatest value of genetic data is accessibility over time, allowing for prospective research and a priori research acting on incidental findings.[190]

As expected for research in for-profit entities, universities and research organisations, DTCGT companies protect their discoveries through patenting. DTCGT patenting though has proven controversial as it generates tension between DTCGT companies' mission of 'democratising genetics' and the reality of 'commercialising genetics'.[191] DTCGT patenting clearly illustrates the

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[186] Heidi Howard, Bartha Knoppers and Pascal Borry, 'Blurring lines' (2010) 11(8) *EMBO reports* 579-582, 579.
[187] Ibid 582.
[188] See <https://www.23andme.com/privacy/> and <https://www.23andme.com/about/consent/>. Research aimed at scientific publication obtains ethics approval from IRB Ethical and Independent Review Services <www.eandireview.com>.
[189] See Emilia Niemiec and Heidi Howard, 'Ethical issues in consumer genome sequencing: Use of consumers' samples and data' (2016) 8 *Applied & Translational Genomics* 23-30; Jeantine Lunshof, Ruth Chadwick, Daniel Vorhaus and George Church, 'From genetic privacy to open consent' (2008) *Nature Reviews Genetics* DOI: 10.1038.nrg2360.
[190] Courtney Kronenthal, Susan Delaney and Michael Christman, 'Broadening research consent in the era of genome-informed medicine' (2012) 14(4) *Genetics in Medicine* 432-436.
[191] See Megan Allyse, '23and Me, We, and You: direct-to-consumer genetics, intellectual property, and informed consent' (2013) 31(2) *Trends in Biotechnol* 68-69; Sigrid Sterckx, Julian Cockbain, Heidi Howard and Pascal Borry, 'I prefer a child with ...: Designer babies, another controversial patent in the arena of direct-to-consumer genomics' (2013) 15 *Genetics in Medicine* 923-924.

difference between science for shareable discoveries as exemplified in the Human Genome Project and science for exclusive profitability.

### *Concerns about DTCGT's impact on individuals warranting further investigation*

The concerns and empirical findings in Part Two form the core of the survey component which seeks to both replicate and extend aspects of existing empirical studies investigating interpretation, affect and behavioural intentions/behavioural change. Overall, the empirical research to date suggests *most* consumers *do not* experience inappropriate affect or engage in inappropriate behaviours. While the focus in existing empirical research has been establishing whether the potential for widespread consumer harm exists, few have focused on those consumers who *do* experience inappropriate affect or engage in inappropriate behaviours, perhaps because of their comparatively small numbers. What is needed is a richer understanding of this particular group, as these are the consumers who may be harmed overall by DTCGT engagement, which this research seeks to provide.

## PART THREE: CONCERNS ABOUT THE IMPACT ON HEALTHCARE SYSTEMS

In the DTCGT environment, consumers are left to 'self-interpret' results, as interpretation and counselling by trained healthcare professionals is generally not a standard component of the DTCGT offering.[192] Concern has been expressed that consumers, uncertain as to interpretation or management options, will turn to the healthcare system for assistance.[193]

Two key areas of concern relative to DTCGT's impact on healthcare systems are discussed: whether individuals armed with DTCGT results will share with doctors, and whether healthcare professionals, including genetic specialists, are ready for DTCGT.

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[192] See Heidi Howard and Pascal Borry, 'Survey of European clinical geneticists on awareness, experiences and attitudes towards direct-to-consumer genetic testing' (2013) 5 *Genome Medicine* 45-56; Amy McGuire, Christina Diaz, Tao Wang and Susan Hilsenbeck, 'Social Networkers' Attitudes Toward Direct-to-Consumer Personal Genome Testing' (2009) 9(6-7) 3-10.

[193] See Gemma Brett, Sylvia Metcalfe, David Amor and Jane Halliday, 'An exploration of genetic health professionals' experience with direct-to-consumer genetic testing in their clinical practice' (2012) 20 *European Journal of Human Genetics* 825-830; Monica Giovanni, Matthew Fickle, Lisa Lehman, Robert Green, Lisa Meckley, David Veenstra and Michael Murphy, 'Health-care Referrals from Direct-to-Consumer Genetic Testing' (2010) 14(6) *Genetic Testing and Molecular Biomarkers* 817-819.

### 4.3.1 Sharing with doctors: Company and consumer-initiated engagement

Concern has been expressed DTCGT testing may place 'a substantial burden on the health care system without providing demonstrable benefit'[194] needlessly stretching overburdened doctors 'already struggling to care for those with increasingly complex diseases.'[195] Engagement with healthcare is not cost-neutral if, as Caulfield suggests, consumer pay for obtaining genetic information but then access 'the publicly financed system for interpretive help.'[196] Modelling of the DTCGT space in Chapter Three (3.2.3) identified engagement with health-care systems could be initiated either by consumers themselves or DTCGT companies.

#### 4.3.1.1 Consumer-initiated engagement

Trust in sources of health information varies, with higher levels resulting in increased likelihood of sharing and, most importantly, actioning recommendations.[197] As trust in doctors is relatively high in Australia and the US, it would be expected individuals confused or distressed post-DTCGT would seek their assistance.[198] This would be consistent with existing usage patterns – on an average day 406,000 visits are made to Australia's GPs.[199] Early research suggested the majority of potential consumers would seek professional assistance with interpretation and believed physicians have a professional responsibility to interpret DTCGT results.[200]

Seeking medical advice may prompt pre-symptomatic vigilance such as screening for those at risk or referral to specialists resulting in early diagnosis leading to more patient-efficient and cost-

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[194] Justin Annes, Monica Giovanni and Michael Murray, 'Risks of presymptomatic direct-to-consumer genetic testing' (2010) 363(12) *New England Journal of Medicine* 1100-1101, 1101.
[195] James Meikle 'Superdrug criticized by doctors for stocking genetic self-testing kits' (2015) 1 April *The Guardian* <https://www.theguardian.com/science/2015/mar/31/superdrug-criticised-doctors-genetic-self-testing-kits>. Quoting Maureen Baker, chair of UK Royal College of General Practitioners.
[196] Timothy Caulfield, 'Direct-to-consumer genetics and health policy? A worst-case scenario' (2009) 9 (6-7) *The American Journal of Bioethics* 48-50, 49.
[197] See Laura Sbaffi and Jennifer Rowley, 'Trust and Credibility in Web-based Health Information: A Review and Agenda for Future Research' (2017) 19(6) *Journal of Medical Internet Research* DOI:10.2196/jmir.7579; Rob Lawson, Sarah Forbes and John Williams, 'Patterns of trust in sources of health information, (2011) 124(1328) *The New Zealand Medical Journal* <https://nzma.org.nz/journal>.
[198] See Robert Blendon, John Benson and Joachim Hero, 'Public Trust in Physicians − U.S. Medicine in International Perspective' (2014) 371(17) *New England Journal of Medicine* 1570-1572. Australia ranked 10th with 73% and the US 24th with 56% expressing trust in doctors.
[199] See also Australian Institute of Health and Welfare, *Australia's Health 2018: In brief* (2018) Cat. no AUS222: Canberra, AIHW, 3.
[200] Amy McGuire, Christina Diaz, Tao Wang and Susan Hilsenbeck, 'Social Networkers' Attitudes Toward Direct-to-Consumer Personal Genome Testing' (2009) 9(6-7) 3-10.

effective outcomes than symptomatic interventions.[201] The opportunity for patient-doctor dialogue may also increase patient understanding and reduce anxiety, circumventing potentially longer-term mental health issues.[202] Engagement with healthcare may not only prompt appropriate behavioural changes but also circumvent independent inappropriate behavioural changes, such as changing medications.

Importantly, once individuals seek expert opinion, they enter the medical sphere becoming *patients* rather than *consumers*, afforded full medico-legal protections. As noted however, 'it would be a 'very brave' GP who relied on the results of a DTCGT test to manage a patient.'[203] Australia's NHMRC 2013 guidance for healthcare professionals is clear: 'Direct-to-consumer genetic tests should not be used as the basis for clinical decision making and health care.'[204] This raises the issue of physician liability relative to interpreting DTCGT results and dealing with patients presenting with slightly increased risk on tests detecting low-risk factors where there are no medically accepted preventative measures.[205] In these situations, doctors are left to determine the level of risk triggering either confirmatory testing or referral to costly specialist services, which, while reducing liability, may 'impose unnecessary cost and time burdens on health care systems'.[206]

#### *4.3.1.2 Company-initiated engagement*

While most DTCGT companies make concerted efforts to avoid exercising medical judgement and charges of unlicensed practice of medicine, encouraging seeking medical advice, others blur the

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[201] See D Boeldt, N Schork, E Topol and C Bloss, 'Influence of individual differences in disease perception on consumer response to direct-to-consumer genomic testing' (2015) 87 *Clin Genet* 225-232 (higher genetic risk increased likelihood of seeking expert opinion); Karen Powell, Whitney Cogswell, Carol Christianson, Gaurav Dave, Amit Verma, Sonja Eubanks and Vincent Henrich, 'Primary care physicians' awareness, experience and opinions of direct-to-consumer genetic testing' (2012) 21 *J Genet Counsel* 113-126.

[202] See The Royal Australian College of General Practitioners, *General Practice: Health of the Nation 2018* (2018) <https://www.racgp.org.au/download/Documents/Publications/Health-of-the-Nation-2018-Report.pdf>; Deanna Carere, Peter Kraft, Kimberly Kaphingst, Scott Roberts and Robert Green, 'Consumers report lower confidence in their genetics knowledge following direct-to-consumer personal genomic testing' (2016) 18(1) *Genetics in Medicine* 65-71.

[203] Cathy Johnson 'Angelina Jolie triggers gene test warning', 23 May 2013 The Pulse, abc.net.au <http://www.abc.net.au/health/thepulse/stories/2013/05/23/3765907.htm>. Quoting Professor Graeme Suther, then Chair Genetics Advisory Committee of the Royal College of Pathologists of Australasia.

[204] Australian Government, NHMRC, 'Discussing Direct-to-Consumer Genetic DNA Testing with Patients' (2013) NHMRC REF #G7, 3.

[205] Stephanie Bair, 'Direct-to-consumer genetic testing: Learning from the past and looking forward to the future' (2012) 67 *Food and Drug Law Journal*, 413-433.

[206] See Amy McGuire and Wylie Burke, 'Health system implications of direct-to-consumer personal genome testing' (2011) 14 *Public Health Genomics* 53-58, 56.

boundaries.[207] Navigenics, an early player, introduced the business model of company-initiated engagement with doctors. Some DTCGTs now combine traditional DTCGT marketing and e-commerce efforts directed at consumers, with either compulsory or voluntary results returns to doctors or the requirement either in-house company or personal doctors order tests.[208] One example is Sema4, which requires in-house clinical approval before online sale of its CarrierScreen™. Genetic counselling is available post-results, as the company seeks to 'bridge the gap between consumer demand for genetic testing and the need for medically appropriate oversight and advice' to safeguard consumers'.[209] One has to question though why in-house clinical approval might be denied, given the commercial imperative. On the positive side, both company doctors and company genetic counsellors would be aware of the particulars of each test, although they would also have the accept the implications such knowledge generates e.g. liability/negligence.

This DTCGT business model still relies on consumers to initiate, in essence 'forcing' physicians to become involved. Physician-ordering places needs assessment with physicians, who must determine clinical benefits and risks before ordering,[210] assuming, that is, they can assess the validity of specific DTCGT tests requested by patients.[211] However this may open them to pressure to order and later interpret non-essential tests, especially as DTCGT bundles tests. Results return transfers responsibility and liability to physicians and specialists for interpretation and actioning, affording DTCGT customers the traditional protections offered to *patients*. Also, whether doctor-patient relationships are established between in-house company physicians and consumers has not been definitively established.[212] While adding gatekeepers into the DTCGT process addresses criticisms of lack of medical involvement and allows companies to market to both consumers and

[207] See Jennifer Wagner, 'Interpreting the Implications of DNA Ancestry Tests' (2010) 53(2) *Perspectives in Biology and Medicine* 231-248; Cynthia Marietta and Amy McGuire, 'Direct-to-consumer genetic testing: Is it the practice of medicine?' (2009) 37(2) *J Law Med Ethics* 369-374 DOI:10.111/j.1748-720X.2009.00380.x.
[208] Heidi Howard and Pascal Borry, 'Is there a doctor in the house? The presence of physicians in the direct-to-consumer genetic testing context' (2012) 3 *J Community Genet*, 105-112.
[209] Anon, 'Sema4 partners with PWNHealth to enable genetic testing for consumers nationwide', 25 September 2017, <https://www.businesswire.com/news/home/20170925005235/en/Sema4-Partners-PWNHealth-Enable-Genetic-Testing-Consumers>.
[210] See Cynthia Marietta and Amy McGuire, 'Direct-to-consumer genetic testing: Is it the practice of medicine?' (2009) 37(2) *J Law Med Ethics* 369-374.
[211] Ronald Trent, 'Direct-to-consumer genetic testing − clinical considerations' (2013) 198(9) *MJA* 496-498.
[212] Cynthia Marietta and Amy McGuire, 'Direct-to-consumer genetic testing: Is it the practice of medicine?' (2009) 37(2) *J Law Med Ethics* 369-374.

physicians,[213] it appears at odds with DTCGT's key promise of removing interaction with traditional gatekeepers facilitating consumer autonomy, empowerment and privacy.[214]

#### *4.3.1.3 Seeking expert opinion – empirical results*

A number of empirical studies have investigated whether actual and potential consumers have, or intend to, engage with healthcare professionals. Meta-analysis by both Stewart et al. and Covolo et al. found overall about one-third of DTCGT customers actually sought expert opinion, despite higher intentions, with Stewart et al. reporting about 10% having subsequent preventative screening.[215]

##### *Actual engagement – DTCGT customers*

PGen researchers found, while 63% planned to share with their doctors, only 27% had at the 6-month follow-up, with those not sharing stating results were not important enough or lacked time. While most discussing with primary care physicians were satisfied, one in five were not, with many citing a lack of engagement or interest by doctors. Researchers concluded whether individuals share might be related to perceptions results can potentially affect their care.[216] Only 4% either made or planned to make appointments with genetic counsellors although 38% would have used them if available as part of the DTCGT offering.[217]

The Hopkins study reported almost one-third shared results with healthcare professionals, mostly primary care providers. Of those sharing, approximately half reported learning something useful from their test results and 10% having additional lab tests, more likely for those with family histories, although it is unclear whether testing resulted in early detection or patient

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[213] See Heidi Howard and Pascal Borry, 'Is there a doctor in the house? The presence of physicians in the direct-to-consumer genetic testing context' (2012) 3 *J Community Genet*, 105-112.
[214] Heidi Howard and Pascal Borry, 'Direct-to-consumer pharmacogenomic testing' (2011) 12(10) *Pharmacogenomics* 1367-1370.
[215] Kelly Stewart, Anke Wesselius, Maartje Schrerurs, Annemie Schols and Maurice Zeegers, 'Behavioural changes, sharing behaviour and psychological responses after receiving direct-to-consumer genetic test results: a systematic review and meta-analysis' (2018) 9(1) *J Community Genet* 1-18; Loredana Covolo, Sara Rubinello, Elisabetta Ceretti and Umberto Gelatti, 'Internet-based direct-to-consumer genetic testing: A systematic review' (2015) 17(12) *J Med Internet Res* DOI: 10.2196/jmir.4378 (118 articles).
[216] Cathelijne van der Wouden, Deanna Carere, Anke Matiland-van der Zee, Mack Ruffin, Scott Roberts and Robert Green, 'Consumer perceptions of interactions with primary care providers after direct-to-consumer personal genomic testing' (2016) *Annals of Internal Medicine* DOI: 10.7326/M15-0995.
[217] Diane Koeller, Wendy Uhlmann, Deanna Carere, Robert Green and Scott Roberts, 'Utilization of genetic counseling after direct-to-consumer-genetic testing: Findings from the Impact of Personal Genomics (PGen) study' (2017) 26 *J Genet Counsel* 1270-1279.

reassurance.[218] Scripps researchers found almost one-third sought physician advice six months post-testing and over one-third post one year.[219] Higher physician utilisation was also found in response to pharmacogenomic results with 'no adverse changes in psychological health or follow-up test-related distress.'[220] Over 80% also shared pharmacogenomic results with family, suggesting testing may lead to '…health-related discussions within families and promote more accurate knowledge of family disease and prescription drug use histories.'[221] Even though Navigenics provided free genetic counselling to Scripps participants, 14 months post-testing only 14% had used the service, with most doing it to either to take advantage of the free service or obtain more information about risk calculations. Positively, the majority indicated consultations improved their understanding of both genetics and DTCGT results. Of those not consulting, the majority believed it was not necessary as they were confident they understood results.[222]

Similar results were found by Gollust et al. with 92% of individuals taking non-DTCGT genetic tests stating an intention to seek expert recommendations post-test, with only 15% actually consulting doctors six months post-test and intention falling to 50%.[223] Reid et al. found increased physician utilisation pre-test but no subsequent change post-test.[224]

### *Intention to engage – potential DTCGT customers*

Intention was high in response to hypothetical DTCGT results, with McGuire et al. reporting 78% of those intending to purchase would consult physicians, Leighton et al. 85%, and Bansback et al.

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[218] David Kaufman, Juli Bollinger, Rachel Dvoskin and Joan Scott, 'Risky Business: Risk Perception and the Use of Medical Services among Customers of DTCGT Personal Genetic Testing' (2012) 21 *Journal of Genetic Counseling* 413-422.

[219] Burcu Darst, Lisa Madlensky, Nicholas Schork, Eric Topol and Cinnamon Bloss, 'Characteristics of genomic test consumers who spontaneously share results with their health care provider' (2014) 29(1) *Health Commun* DOI: 10.1080/10410236.2012.717216; Cinnamon Bloss, Nathan Wineinger, Burcu Darst, Nicholas Schork and Eric Topol, 'Impact of direct-to-consumer genomic testing at long term follow-up' (2013) 50 *Journal of Medical Genetics* 393-400.

[220] Cinnamon Bloss, Nicholas Schork and Eric Topol, 'Direct-to-consumer pharmacogenomic testing is associated with increased physician ultilisation' (2014) 51 *Journal of Medical Genetics* 83-89, 83.

[221] Ibid 88.

[222] Burcu Darst, Lisa Madlensky, Nicholas Schork, Eric Topol and Cinnamon Bloss, 'Perceptions of genetic counseling services in direct-to-consumer personal genomic testing' (2013) 84 *Clinical Genetics* 335-339.

[223] Sarah Gollust, E Gordon, C Zayac, G Griffin, M Christman, R Pyeritz, L Wawak and B Bernhardt, 'Motivations and Perceptions of Early Adopters of Personalized Genomics: Perspectives from Research Participants' (2012) 15 *Public Health Genomics* 22-30 (369 individuals recruited from the non-DTCGT Coriell Personalised Medicine Collaborative).

[224] Robert Reid, Colleen McBride, Sharon Hensley Alford, Cristofer Price, Andreas Baxenvanis, Lawrence Brody and Eric Larson, 'Association between health service use and multiplex genetic testing' (2012) 14(16) *Genet Med* 852-859 (1559 members of non-DTCGT Multiplex Initiative).

63%.[225] Rollins et al. found those perceiving greater disease threat in response to mock DTCGT advertisements reported significantly higher intentions.[226] Interestingly, McGuire et al. found while the majority believed physicians have a professional responsibility to interpret DTCGT results, only 47% felt doctors had enough genetics knowledge. On a positive note, McBride et al. concluded individuals presenting DTCGT results to doctors may be 'among the most motivated to take steps towards healthier lifestyles.'[227]

The empirical research found intention to engage did not substantively translate into actual engagement, nor were test results used to undergo unnecessary testing or inappropriately behaviours.[228] The key word however is 'substantive'. If the DTCGT market expands as forecast, the one-third of consumers seeking expert opinion will represent an increasingly larger absolute number. It must also be noted empirical research to date reflects primarily the opinions and experiences of early adopters. As acknowledged by researchers themselves, whether other market segments will exhibit the same patterns remains to be seen.[229]

### *4.3.2 Expertise: Are healthcare professionals ready for DTCGT?*

Regardless of numbers, or whether engagement is consumer or company-initiated, the key question is whether healthcare professionals are able to first understand, and then accurately interpret DTCGT results in order to provide informed advice to *patients* relative to lifestyle,

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[225] Nick Bansback, Sonia Sizto, Daphne Guh and Aslam Anis, 'The Effect of Direct-to-Consumer Genetic Tests on Anticipated Affect and Health-Seeking Behaviors: A Pilot Survey' (2012) 16(10) *Genetic Testing and Molecular Biomarkers* 1165-1171; Justin Leighton, K Valverde and B Bernhardt, 'The General Public's Understanding and Perception of Direct-to-Consumer Genetic Test Results' (2011) *Public Health Genomics* 11-21 (Facebook survey of 145 members of general public and 171 genetic counsellors); Amy McGuire, Christina Diaz, Tao Wang and Susan Hilsenbeck, 'Social Networkers' Attitudes toward Direct-to-Consumer Personal Genome Testing' (2009) 9(6-7) *The American Journal of Bioethics* 3-10 (1087 general public members recruited through online market research panels).

[226] Brent Rollins, Shravanan Ramakrishnan and Matthew Perri, 'Direct-to-consumer advertising of predictive genetic tests: A health belief model based on examination of consumer response' (2014) 31 *Health Marketing Quarterly* 263-278.

[227] Colleen McBride, Sharon Alford, Robert Reid, Eric Larson, Andreas Baxevanis and Lawrence Brody, 'Characteristics of users of online personalized genomic risk assessments: Implications for physician-patient interactions' (2009) 11(8) *Genetics in Medicine* 582-587, 582.

[228] See Kelly Stewart, Anke Wesselius, Maartje Schrerurs, Annemie Schols and Maurice Zeegers, 'Behavioural changes, sharing behaviour and psychological responses after receiving direct-to-consumer genetic test results: a systematic review and meta-analysis' (2018) 9(1) *J Community Genet* 1-18; M Barton, 'Health behaviours not significantly changed by direct-to-consumer genetic testing' (2017) 67(3) *CA Cancer J Clin* 175-176; Robert Green and Nita Farahany, 'The FDA is overcautious on consumer genomics' (2014) 505 *Nature* 286-287.

[229] See Cecile Janssens, 'The hidden harm behind the return of results from personal genome services: a need for rigorous and responsible evaluation' (2014) 20 November *Genetics in Medicine* DOI: 10.1038/gim.2014.169.

medical and pharmaceutical interventions.[230] By their own admission, the answer is no – for both clinical and DTCGT genetic tests. Delaney and Christman concluded relative to DTCGT, 'Physician preparedness is not currently as promising as patient readiness.'[231] The Human Genetics Society of Australasia clearly states, to support informed choices, that 'adequate and ongoing education and resources should be available for consumers and health care professionals before, during and after testing.'[232]

#### *4.3.2.1 Doctors*

The need for increased focus on genetics education for medical students, public health officials and primary care physicians is a recurring theme in the literature, with Goldsmith et al. concluding it is 'generally acknowledged that knowledge of genetics in health professionals is low'.[233]

From the doctors' perspective, many Australian GPs felt inadequately prepared to manage genetic conditions and rated their overall genetics knowledge as poor.[234] Only one in five US physicians believed genetics training was sufficient with under 20% very confident interpreting genetic test results.[235] From the patients' perspective, an early study found 64% of patients with genetic conditions did not receive genetics-education materials from their primary care providers, with respondents rating their own genetic knowledge and those of genetic specialists as higher than that of primary care providers.[236]

Powell et al. found only 15% of primary care physicians felt adequately prepared to discuss DTCGT results with patients but 74% were eager to learn, while Bernhardt et al. reported under 10% had

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[230] See Ronald Trent, 'Direct-to-consumer DNA genetic testing and the GP' (2014) 43(7) *Australian Family Physician* 436-439.
[231] Susan Delaney and Michael Christman, 'Direct-to-consumer genetic testing: perspectives on its value in healthcare' (2016) Feb/Mar *Clinical Pharmacology and Therapeutics* DOI: 10.1002/cpt.287.
[232] Human Genetics Society of Australasia, *Position Statement: Online DNA Testing* (2018) 2018 PSO2.
[233] Lesley Goldsmith, Leigh Jackson, Anita O'Connor and Heather Skirton, 'Direct-to-consumer genomic testing from the perspective of the health professional: a systematic review of the literature' (2013) 4 *J Community Genet* 169 − 180, 172. See also Michael Wolyniak, Lynne Bemis and Amy Prunuske, 'Improving medical students' knowledge of genetic disease: a review of current and emerging pedagogical practices' (2015) 6 *Advances in Medical Education and Practice* 597-607; Grant Blashki, Sylvia Metcalfe and Jon Emery, 'Genetics in general practice' (2014) 43(7) *Australian Family* Physician 428-431.
[234] Sylvia Metcalfe, Rosalind Hurworth, Jennifer Newstead and Rosemary Robins, 'Needs assessment study of genetics education for general practitioners in Australia' (2002) 4(2) *Genetics in Medicine* 71-77.
[235] Barbara Bernhardt, Cara Zayac, Erynn Gornon, Lisa Wawak, Reed Pyeritz and Sarah Gollust, 'Incorporating direct-to-consumer genomic information into patient care: attitudes and experiences of primary care physicians' (2012) 9(7) *Personalized Medicine* 683-692.
[236] Erin Harvey, Chana Fogel, Mark Peyrot, Kurt Christensen, Sharon Terry and Joseph McInerney, 'Providers' knowledge of genetics: A survey of 5915 individuals and families with genetic conditions' (2007) 9(5) *Genetics in Medicine* 259-267.

actually seen a DTCGT report.[237] McGuire and Burke suggest low physician familiarity would result in inefficient use of limited time with patients, and could have a cascade effect where 'ambiguous, incidental, or false-positive results' lead to additional testing or over-diagnosis.[238] Peterson et al. concluded overall doctors reported 'insufficient knowledge and overall caution, particularly regarding direct-to-consumer testing', prompting Bernhardt et al. to note the need for additional physician education relative to new genomic techniques and knowledge is 'unquestioned'.'[239] Schleckser suggests physicians need specifically to understand how genetic markers are selected and genetic risk reported by DTCGTs and the impact of 'missing' information such as environmental factors.[240]

#### *4.3.2.2 Genetic specialists*

Clinical geneticists are doctors with specialised training in diagnosing and treating genetic conditions and genetic counsellors are specially trained to provide support to patients with genetic issues. However, currently both are in limited supply in Australia.

Research suggests less than 10% of Australasian genetic counsellors and clinical geneticists reported being confident in accurately interpreting or explaining DTCGT test results. The small number with DTCGT experience reported 80% of clients needed interpretation assistance, 76% reported tests created anxiety, and considered only one-third of tests presented as having clinical benefit.[241] Giovanni et al. found while half of genetic counsellors with DTCGT experience deemed

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[237] Karen Powell, Carol Christianson, Whitney Cogswell, Gaurav Dave, Amit Verma, Sonja Eubanks and Vincent Henrich, 'Educational Needs of Primary Care Physicians Regarding Direct-to-Consumer Genetic Testing' (2012) 21 *J Genet Counsel* 469-476; Barbara Bernhardt, Cara Zayac, Erynn Gornon, Lisa Wawak, Reed Pyeritz and Sarah Gollust, 'Incorporating direct-to-consumer genomic information into patient care: attitudes and experiences of primary care physicians' (2012) 9(7) *Personalized Medicine* 683-692.

[238] Amy McGuire and Wylie Burke, 'An unwelcome side effect of direct-to-consumer personal genome testing: Raiding the medical commons' (2008) 300(22) *JAMA* 2669-2671, 2669. See also Amy McGuire and Wylie Burke, 'Health system implications of direct-to-consumer personal genome testing' (2011) 14 *Public Health Genomics* 53-58.

[239] Emily Peterson, Wen-Ying Chou, Anna Gaysynsky, Melinda Krakow, Ashley Elrick, Muin Khoury and Kimberly Kaphingst, 'Communication of cancer-related genetic and genomic information: A landscape of reviews' (2018) 8 *TBM* 59-70, 59 (24 articles from 2010 – 2018); Barbara Bernhardt, Cara Zayac, Erynn Gornon, Lisa Wawak, Reed Pyeritz and Sarah Gollust, 'Incorporating direct-to-consumer genomic information into patient care: attitudes and experiences of primary care physicians' (2012) 9(7) *Personalized Medicine* 683-692, 689.

[240] Kathryn Schleckser, 'Physician participation in direct-to-consumer genetic testing: Pragmatism or Paternalism?' (2013) 26(2) *Harvard Journal of Law & Technology* 696-730.

[241] Gemma Brett, Sylvia Metcalfe, David Amor and Jane Halliday, 'An exploration of genetic health professionals' experience with direct-to-consumer genetic testing in their clinical practice' (2012) 20 *European Journal of Human Genetics* 825-830 (130 members Human Genetics Society of Australasia).

results clinically useful, estimating downstream costs to patients, insurers and healthcare systems for subsequent referral and testing between US$40-$20,600.[242]

An earlier US study found over half of genetic counsellors believed they had a professional responsibility to both be knowledgeable about and able to interpret DTCGT results, with the majority prepared to recommend DTCGT to patients with concerns about genetic discrimination, wanting anonymous testing, or experiencing geographic constraints.[243] Wade and Wilford suggest that 'Genetic counselors' obligations to care for clients extends to interpreting DTCGT tests, although this obligation could be fulfilled by referral or consultation with specialists.'[244]

Middleton et al. note in particular the lack of pre-test counselling, suggesting eventually customers will present experiencing 'tangible psychological damage from the results of tests linked to serious, life-threatening conditions.'[245] While suggesting DTCGTs themselves should provide support and not rely on healthcare systems, they note 'companies have no vested interest in discovering whether their tests cause psychological or physical harm.'[246]

### *Concerns about DTCGT's impact on the healthcare system warranting further investigation*

Healthcare professionals, especially primary care, recognise their knowledge and experience with DTCGT is inadequate to prepare them for patients presenting with DTCGT results seeking interpretation assistance and advice. Preparing the healthcare system to engage with DTCGT has significant cost implications including training, confirmatory testing and psychosocial interventions such as counselling, and could potentially divert public funds from other initiatives. However, the critical first step is to determine if consumers intend to bring DTCGT results to doctors and their volume, as this will dictate the amount and urgency of preparation. To date, no Australian studies have looked at behavioural intention to share with healthcare in response to DTCGT results, warranting further investigation.

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[242] Monica Giovanni, Matthew Fickle, Lisa Lehmann, Robert Green, Lisal Meckley,David Veenstra and Michael Murray, 'Health-care referrals from direct-to-consumer genetic testing' (2010) 14(6) *Genetic Testing and Molecular Biomarkers*, 817-819 (131 clinical geneticists reporting on 22 DTCGT cases).
[243] Kathryn Hock, Kurt Christensen, Beverly Yashar, Scott Roberts, Sarah Gollust and Wendy Uhlmann, 'Direct-to-consumer genetic testing: An assessment of genetic counselors' knowledge and beliefs' (2011) 13(4) *Genetics in Medicine* 325-332.
[244] Christopher Wade and Benjamin Wilford, 'Ethical and clinical practice considerations for genetic counsellors related to direct-to-consumer marketing of genetic tests' (2006) 142C *American Journal of Medical Genetics Part C (Seminars in Medical Genetics)* 284-292, 284. See also Alice Hawkins and Anita Ho, 'Genetic counselling and the ethical issues around direct to consumer genetic testing' (2012) 21 *J Genet Counsel* 367-373.
[245] Anna Middleton, Alvaro Mendes, Caroline Benjamin and Heidi Howard, 'Direct-to-consumer genetic testing: where and how does genetic counselling fit?' (2017) 14(3) *Personalized Medicine* 249-257, 254.
[246] Ibid 255.

## CONCLUSION: THE COST OF EMPOWERMENT FOR THE MANY MAY BE HARM FOR THE FEW

The volume of academic literature, government, organisational and industry reports as well as mass media representations can be summed up in two key themes: the potential for *consumer empowerment* and the potential for *consumer harm*.

When the empirical research is viewed as a whole, '… the speculated harms have not, in general, materialized to the degree often suggested in the realm of popular discourse.' [247] While widespread test misunderstanding and psychological distress have not eventuated, and healthcare systems have not been unduly burdened from unnecessary clinical follow-up, neither has the promised widespread consumer empowerment with its positive and sustained health benefits occurred.[248]

While scientific and empirical studies suggest *most* tests are accurate, and *most* individuals do interpret results in a manner consistent with their actual DTCGT results, this also means that *some* tests aren't accurate, and *some* consumers' interpretations aren't consistent. The potential for harm for the few and its flow-on effects should not be underestimated. Consider the case of an American female with two first-degree relatives with breast cancer. CGT identified a heterozygous pathogenic BRCA2 variant and pre and post-test counselling allowed her to implement appropriate medical care. One year later, the gift of a DTCGT kit revealed she had lower than average risk of breast cancer and did not test positive for either of the BRCA markers, albeit with the company caveat that tests weren't exhaustive. The $5000 test said she was positive, the $99 test said she wasn't. If she had taken the DTCGT first, she may have been falsely reassured and may not have sought medical care until symptomatic.[249]

Determining and quantifying harm is challenging, as harm typically does not result in adverse events requiring documentation and reporting e.g. surgical complications or adverse medical

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[247] Timothy Caulfield, Subhashini Chandrasekharan and Robert Book-Deegan, 'Harm, hype and evidence: ELSI research and policy guidance' (2013) 5(21) *Genome Medicine* <http://genomemedicine.com/content/5/2/21>.

[248] See Cecile Janssens, 'Premature genetic tests did not impact health behaviour' (2016) 29 March *BMJ* <https://www.bmj.com/content/352/bmj.i1102/rapid-responses>; Scott Roberts and Jenny Ostergren, 'Direct-to-consumer genetic testing and personal genomics services: A review of recent empirical studies' (2013) 1 *Curr Genet Med Rep* 182-200; Theresa Marteau, David French, Simon Griffin, A T Prevost, Stephen Sutton, Claire Watkinson, Sophie Attwood, and Gareth Hollands, 'Effects of communicating DNA-based disease risk estimates on risk-reducing behaviours' (2010) 10 *The Cochrane Library* 1-74.

[249] Jennifer Schleit, Lorraine Naylor and Fuki Hisama, 'First, do not harm: direct-to-consumer genetic testing' (2018) 14 June *Genetics in Medicine* DOI:10.1038/s41436-018-0071-z.

reactions.[250] Rather, harm is an individual phenomenon, so determining and quantifying requires individuals to first determine they have been harmed and then disclose at their personal discretion. If individuals over or under-estimate risk, they may not realise they, or those they share with, are being harmed by unjustified affect and they are engaging in inappropriate behaviours.

Lastly, *NO evidence of harm* does not mean *evidence of NO harm*. Empirical research looks at averages and proportions and the majority of respondents neither experienced significant psychological distress nor engaged in inappropriate, or indeed proactive, health behaviours. However, even in studies of early adopters, a small proportion reported *unjustified* affect and *inappropriate* behavioural responses. And reasonably substantial proportions indicated their intention to engage or actual engagement with healthcare providers who, by their own admission, are not prepared for DTCGT. Whether these proportions change or not remains to be seen, the absolute number will increase if the DTCGT market expands as projected.

All empirical studies discussed have limitations, with many of those reported having small sample sizes of primarily US respondents recruited via convenience sampling. Direct comparison between the studies is difficult as each focus on difference aspects of DTCGT engagement, and so must be approached with caution. The most robust and substantive empirical studies studying actual DTCGT consumers reported on reactions of early adopters who it has been suggested 'understand the limited predictive impact of DTCGT results and do not over-react either emotionally or in terms of generating additional and unnecessary medical expenses'[251] and 'will not disproportionately exhibit dispositional characteristics commonly associated with negative emotional response.'[252] Other groups or the general public taken as a whole, especially in other jurisdictions, may still experience adverse effects.

Empirical studies to date have also tended to focus on specific aspects of the DTCGT experience, each from different sets of respondents, each applying a different lens, generating a somewhat fragmented view of DTCGT. By interjecting comparative empirical data investigating the key

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[250] See Jennifer Schleit, Lorraine Naylor and Fuki Hisama, 'First, do not harm: direct-to-consumer genetic testing' (2018) 14 June *Genetics in Medicine* DOI:10.1038/s41436-018-0071-z; M Broadstock, S Michie and T Marteau, 'Psychological consequences of predictive genetic testing: a systematic review' (2000) 8 *Eur J Hum Genet.* 731-738.

[251] Brigham and Women's Hospital, 'Studies probe value and impact of direct-to-consumer genetic testing' (2016) 13 December *ScienceDaily* <https://www.sciencedaily.com/releases/2016/12/161213174952.htm>.

[252] Ryan Paquin, Adam Richards, Laura Koehly and Colleen McBride, 'Exploring dispositional tendencies to seek online information about direct-to-consumer genetic tests' (2012) 2(4) *Transl Behav Med.* 392-400, 392.

aspects of consumer engagement and related aspects such as personal, healthcare and company sharing, the research strives assist in the development of a less fragmented of DTCGT's potential empowerment and harm amongst members of the general public. In particular, the survey focuses on gaining as much insight as possible into those consumers who may be harmed. As data is gathered from comparable cohorts across different jurisdictions, inter-jurisdictional comparisons are facilitated. The survey component, discussed in Chapters Five (methodology) and Six (results), hopefully adds a more holistic perspective to the debate seeking to determine whether DTCGT is 'good, bad or benign'.[253]

[253] Timothy Caulfield, Nola Ries, P Ray and C Shuman, 'Direct-to-consumer genetic testing: good, bad or benign?' (2009) *Clinical Genetics* DOI: 10.111/j.1399-004.2009.01291.x.

# Chapter Five:

# Survey methodology: Investigating consumer engagement with DTCGT

# INTRODUCTION

*'It is critical that well-considered research be undertaken to more fully understand and anticipate the responses of individuals given such information which can be highly complex, difficult to interpret, and possibly disturbing.'*[1]

In their review of existing empirical studies of direct-to-consumer health-related genetic testing (DTCGT), Roberts and Ostergren noted specifically the need for more data to determine whether existing regulations appropriately balance consumer and commercial sovereignty with public health safeguards, and to guide both practice and policy in this rapidly evolving area.[2] They suggested, in particular, the need for data concerning consumer psychological and behavioural responses to test results and experiences of healthcare professionals involved.

As discussed in the Introduction to this research (Chapter 1, 1.2), three different research methods were employed: doctrinal analysis of applicable legislation and case law in both medical and consumer spheres; modelling of the DTCGT space based on in-depth review of the offerings and business models of existing players; and empirical research. This latter component is the focus of this chapter, which outlines the decisions made in development of the survey instrument with its embedded experimentation. The survey's overarching objective is to provide data investigating consumer engagement with DTCGT. It focuses on how test results are interpreted, how such interpretation influences both psychological responses and behavioural intentions to engage in proactive health behaviours, involve healthcare professionals, and share with family, online communities and DTCGT companies.

This seeks to fill a gap in the expanding body of empirical studies by collecting data contemporaneously from a large-scale population-based survey of Internet-literate members of the Australian and US general publics. This cross-sectional study brings together numerous and often interrelated variables allowing for advanced analysis, focusing specifically on assessing the potential for consumer harm inherent in DTCGT and its potential impact on healthcare systems. The survey instrument was developed specifically to reflect various issues identified the three broad areas of concern identified in the previous chapter: concerns about the DTCGT offering; concerns about the impact on individuals; and concerns about the impact on healthcare systems.

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[1] Maurie Markman, 'Nonphysician-directed genetic testing for a 'perceived' risk', (2015) February *Clinical Oncology News*, <http:www.clinicaloncology.com?PrintArticle.aspx?A_id=29529&D_id=521&D-Provocative+Perspectives_In+Oncology>.

[2] Scott Roberts and Jenny Ostergren, 'Direct-to-consumer genetic testing and personal genomics services: A review of recent empirical studies' (2013) 1 *Curr Genet Med Rep* 182-200.

This chapter reports on the survey methodology employed and is foundational for Chapter Six, providing the context for evaluating survey analysis and results. It is divided into five parts with three accompanying appendices. Part One presents the overall research aim and specific research questions. Part Two details development of the survey instrument and Part Three the specific methods employed. Part Four explains how data was collected and analysed. Importantly, Part Five details the interpretation rules applied, as these must be considered when reviewing results. Appendix Two contains an annotated sample survey, Appendix Three an outline of the statistical tests conducted, and Appendix Four the Confirmatory Factor analysis performed to identify underlying constructs for analysis.

## PART ONE: RESEARCH AIM AND SPECIFIC RESEARCH QUESTIONS

The overarching aim of this component of the research is to identify broad patterns and relationships relative to consumer engagement with the DTCGT offering that were sufficiently substantial, consistent, meaningful and actionable to provide guidance to regulators. Specifically, this empirical component seeks to answer the following broad research questions:

One – Is there potential for psychological detriment resulting from engagement with DTCGT test results?

Two – Is it likely consumers would be exposed to potential psychological detriment through purchase?

Three – Do DTCGT health-related test results motivate intention to change behaviour?

Four – Do DTCGT health-related test results motivate intention to engage with healthcare professionals?

Five – Is there consistent and substantial response variation by country, specific type of test, or selected respondent characteristics?

## PART TWO: DEVELOPING THE SURVEY INSTRUMENT – WHAT TO TEST?

Given the desire to provide a more holistic view looking at key aspects of the DTCGT process, flow-on effects and interrelationships, a survey was determined as the best way to elicit responses to the largest possible number of questions from robust samples across two countries. Constructing surveys involve difficult decisions, as researchers are always cautious the impact instrument length has on both respondent interest and fatigue, limiting what realistically can be included. The survey focuses solely on disease predisposition (the effect of genes on an individual's likelihood of developing particular diseases)[3] and pharmacogenomics (the effect of genes on individual responses to particular drugs).[4]

DTCGT disease predisposition tests were selected as they provide relative risk information, requiring self-interpretation. In the context of pharmacogenomics, while obtaining prescriptions involves engaging with each country's healthcare system, individuals self-manage their administration, with the potential for prescription misuse defined as 'use contrary to the prescribed instructions, without regard to any resulting harm or adverse effect.'[5] This interest stemmed from the 2013 Australian television programme *Heart of the Matter* questioning links between cholesterol and cardiovascular disease, suggesting statin benefits were overstated and harms understated.[6] Doctors expressed concern patients might independently cease or alter statin usage, despite programme advice to the contrary. Subsequent research analysing dispensing records found temporary increases in discontinuation and sustained decreases in statin dispensing, suggesting potential prescription misuse.[7] Concerns about prescription misuse were consistent with US FDA warnings to DTCGTs.[8]

To assess the potential for psychological detriment and resulting behavioural intentions, experiments were crafted using scenarios where key aspects of sample test results were

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[3] Genetics Home Reference, 'What does it mean to have a genetic predisposition to a disease?' <https://ghr.nlm.nih.gov/primer/mutationsanddisorders/predisposition>.
[4] Genetics Home Reference, 'What is pharmacogenomics?' <https://ghr.nlm.nih.gov/primer/genomicresearch/pharmacogenomics>.
[5] Benny Monheit, Danusia Pietrzak and Sandra Hocking, 'Prescription drug – abuse – A timely update', (2016) 45(12) *Australian Family Practitioner* 862.
[6] Australian Broadcasting Corporation, Audience and Consumer Affairs Unit <http://about.abc.net.au/wp-content/uploads/2014/05/Catalyst-Heart-of-the-Matter-ACA-Investigation-Report.pdf>.
[7] Andrea Schaffer, Nicholas Buckley, Timothy Dobbins, Emily Banks and Sallie-Anne Pearson, 'The crux of the matter: did the ABC's *Catalyst* program change statin use in Australia?' (2015) 202(11) *MJA* (2015) 591-595.
[8] For example, FDA warning letter to 23andMe 11/22/13 <https://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm376296.htm>.

manipulated to determine response variation.[9] To assess likely exposure to psychological detriment, purchase likelihood was tested under varying conditions. To determine if responses were respondent-dependent, questions covering personal characteristics (demographics) and personal health status, health-related and DTCGT-specific knowledge, attitudes and behaviours/behavioural intentions were included to allow assessment of particular vulnerabilities. As familiarity with DTCGT could not be assumed, a brief overview of DTCGT health-related testing was provided at the start of the survey to ensure all respondents had sufficient knowledge for survey completion.

Part Two has four components. The first outlines the experiments crafted to determine the potential for psychological detriment. The second outlines how the potential for exposure to psychological detriment was determined with the third detailing additional pre and post-scenario questions. The last discusses survey pre-testing and includes a schematic illustrating overall survey flow. Appendix Two contains an annotated survey showing question order, answer options and randomisation, questions presented per screen, and references for particular questions. The sample survey also notes the specific concerns each question tests.

### 5.2.1 Determining the potential for psychological detriment

Three experiments were conducted with two focusing on disease predisposition testing the influence of risk information and one on pharmacogenomics (hereafter referred to as drug sensitivity).[10] Tests for disease predisposition are predictive not definitive, providing information on an individual's relative risk. Selecting two different diseases allowed for comparative analysis to determine the influence of type of test. Tests for drug responses are definitive, providing individuals with their particular classification or type.

#### 5.2.1.1 Selecting the diseases

The aim in selecting the diseases was to ensure respondents had reasonable awareness and purchase likelihood,[11] diseases were polygenetic with both genetic and environmental risk factors, testing was available both through the medical system and via DTCGT, and each had a significant impact on both the citizens and healthcare systems in Australia and the US. Further, diseases selected had to have lifestyle and/or medical options for risk mitigation and/or

[9] See Rafael Ramirez, Malobi Mukherjee, Simona Vezzoli and Arnoldo Kramer, 'Scenarios as a scholarly methodology to produce interesting research' (2015) 71 *Futures* 70-87.
[10] Unless noted, pharmacogenomics is referred to as Drug sensitivity.
[11] Gordana Bruce and Christine Critchley (2013) *Swinburne National Technology and Science Monitor* <http://apo.org.au/system/files/119126/apo-nid119126-477751.pdf>.

treatment. After analysing a range of diseases, Type 2 Diabetes and Colorectal Cancer were deemed to meet these criteria as discussed below.

### *Type 2 Diabetes*

Type 2 Diabetes represents a significant healthcare challenge in both countries.[12] In 2015, Diabetes was the 6th leading cause of death in Australia and 7th in the US, with lifetime risk of developing the disease increasing.[13] Diabetes Australia refers to Diabetes as 'the epidemic of the 21st century and the biggest challenge confronting Australia's health system', with total annual cost estimated at AU$14.6 billion.[14] The US Centres for Disease Control and Prevention (CDC) estimated the cost of diagnosed diabetes was US$245 billion in 2017.[15] The CDC estimated one-third of US adults had pre-diabetes in 2015, suggesting costs will continue to increase.

As at 31 March 2017, 1,076,970 Australians with Type 2 Diabetes were registered on the Australian National Diabetes Services Scheme, representing approximately 4.5% of the Australian population, with estimates suggesting a further 500,000 Australians were undiagnosed.[16] According to the CDC, 23.1 million Americans have all types of Diabetes, with approximately 7.2 million undiagnosed.[17] As between 90-95% of all Diabetes diagnoses are Type 2, this conservatively amounts to 20.8 million or approximately 6.5% of the US population.[18]

### *Colorectal Cancer*

While incidence and mortality rates have been declining,[19] Colorectal Cancer is the second most commonly diagnosed cancer in Australia[20] and third in US.[21] According to the Australian Institute

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[12] Unless noted, 'diabetes' refers specifically to Type 2 Diabetes and 'cancer' to Colorectal Cancer.
[13] Australian Bureau of Statistics, 3303.0 – Causes of Death, Australia, 2015, released 28/09/2016; National Center for Health Statistics, *Health, United States* 2016, Hyattsville, MD, 2017, 18; Symen Ligthard, Thijs van Herpt, Maarten Leening, Mayam Kavousi, Albert Hofflam, Bruno Stricker, Mandy van Hoek, Eric Sijbrands, Oscar Franco and Abbas Dehghan, 'Lifetime risk of developing impaired glucose metabolism and eventual progression from prediabetes to Type 2 Diabetes: a prospective cohort study' (2016) 4(1) *The Lancet* 44-51.
[14] See <https://www.diabetesaustralia.com.au/diabetes-in-australia>.
[15] US Centres for Disease Control and Prevention, *National Diabetes Statistics Report, 2017*, Atlanta, GA, U.S. Dept of Health and Human Services.
[16] Australian Institute of Health and Welfare, *Australia's Health 2016: In brief* (2016) Cat. no AUS201: Canberra, AIHW, 3; <https://www.diabetesaustralia.com.au/diabetes-in-australia>; Australian Institute of Health and Welfare (2018) *Diabetes compendium* <https://www.aihw.gov.au/reports/diabetes/diabetes-compendium/data>. Based on 2016 population 24.13 million.
[17] US Centres for Disease Control and Prevention, *National Diabetes Statistics Report, 2017*, Atlanta, GA, U.S. Dept. of Health and Human Services.
[18] National Center for Health Statistics, *Health, United States* 2016, Hyattsville, MD, 2017, 23. Based 2016 population of 323.1 million.
[19] See Rebecca Siegel, Kimberly Miller, Stacey Fedewa, Dennis Ahern, Reinier Meester, Afsaneh Bazri and Anmedin Jemal, 'Colorectal Cancer Statistics, 2017' (2017) 67(3) *CA Cancer J Clin* 177-193.

for Health and Welfare, the risk of being diagnosed with Colorectal Cancer by age 85 is 1 in 11 (9.1%) for males and 1 in 15 (6.7%) for females.[22] The American Cancer Society estimates the lifetime risk for males as 1 in 21 (4.7%) and for females 1 in 23 (4.4%).[23] In 2015, Colorectal Cancer was the seventh leading cause of death in Australia,[24] and in 2016 the third leading cause of cancer-related deaths for US females and second leading cause for US males.[25]

Type 2 Diabetes and Colorectal Cancer met the brief as neither disease is solely determined by genetics with family history and lifestyle significant risk factors so DTCGT results provide predictive information only.[26] While Type 2 Diabetes, once diagnosed, can be managed with lifestyle, often in combination with medication, surgical intervention may become necessary. With Colorectal Cancer, in most instances, surgical intervention is required, although lifestyle may both reduce risk and increase likelihood of survival once diagnosed.[27] Both were also judged to be sufficiently high profile to ensure respondent awareness, and of significance in terms of causes of death and costs to the medical systems in each country.

#### *5.2.1.2 Drug sensitivity*

Prescription drugs represent a significant healthcare expenditure in both countries and pharmacogenomic testing for drug sensitivity is available in both healthcare and DTCGT systems. In Australia, the total Pharmaceutical Benefits Scheme government expenditure in the 2015-2016 period was almost AUS$11 billion.[28] In 2015 alone, over 217 million subsidised and 80 million non-

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[20] Australian Institute of Health and Welfare, *Cancer in Australia 2017,* Cancer series no. 101, Cat. no. CAN 100, Canberra: AIHW, 20; Cancer Australia, Australian government *Bowel cancer statistics* <https://bowel-cancer.canceraustralia.gov.au>.
[21] 2017 statistics American Cancer Society <https://www.cancer.org/colon-rectal-cancer/about/key-statistics.html>.
[22] Australian Institute of Health and Welfare, *Cancer in Australia 2017,* Cancer series no. 101, Cat. no. CAN 100, Canberra: AIHW, 21.
[23] American Cancer Society, *Key Statistics for Colorectal Cancer* <https:www.cancer.org/colon-rectal-cancer/about/key statistics.html>; Rebecca Siegel et al, 'Colorectal Cancer Statistics, 2017', (2017) 67(3) *CA Cancer J Clin* 177-193.
[24] Australian Bureau of Statistics, 3303.0 – Causes of Death, Australia, 2015, released 28/09/2016.
[25] American Cancer Society, *Key Statistics for Colorectal Cancer* <https:www.cancer.org/colon-rectal-cancer/about/key statistics.html>; National Center for Health Statistics, *Health, United States* 2016, Hyattsville, MD, 2017, 18.
[26] See <https://www.diabetesaustralia.com.au/type-2-diabetes> and <https://www.cancer.org/cancer/colon-rectal-cancer/causes-risks-prevention/risk-factors.html>.
[27] See Janice Hopkins Tanne, 'Healthy lifestyle leads to better survival in colorectal cancer, study finds', (2018) *BMJ*, DOI: 10.1136/bmj.k1671.
[28] Pharmaceutical Benefits Scheme, *Expenditure and Prescriptions Twelve Months to 30 June 2016* <http://pbs.gov.au/info/browse/statistics>. See also Australian Institute of Health and Welfare, *Australia's Health 2018: In brief* (2018) Cat. no AUS222: Canberra, AIHW, 42.

subsidised prescription drugs were provided to the Australian population.[29] According to the US Center for Medicare and Medicaid Services, US$325 billion was spent on retail prescription drugs in 2015, not including those administered directly by doctors, an amount expected to increase over 6% per year until 2025.[30]

As prescription medications are generally marketed under a range of brand names, a generic blood-thinning drug was selected with a small convenience sample of ten Australians confirming reasonable understanding it was a heart medication intended to thin blood.

#### 5.2.1.3 *Crafting the experiments*

##### *Developing sample DTCGT test results*

The experiments employed scenarios to determine how respondents interpreted and contextualised DTCGT test results, and the impact of these interpretations on psychological outcomes and behavioural intentions. Scenarios have been used in other empirical studies to test risk interpretation and provided the basic structure for the experiments used.[31] This research both replicates aspects of these prior empirical studies while extending them to include contemporaneous data collection in two countries as well as purchase likelihood and resultant flow-on effects.

The experiments for disease predisposition tested three levels of relative risk (one independent variable with three levels) while pharmacogenomics tested two metabolisation rates (one independent variable with two levels).[32] Respondents were randomly allocated into one risk level per disease and one metabolisation rate for drug sensitivity, with quotas imposed to ensure equal distribution across the three sets of scenarios. The overall order was not randomised with all respondents presented their allocated diabetes results the cancer and finally drug sensitivity.

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[29] Commonwealth of Australia, *Australian Statistics on Medicines 2015* <http://www.pbs.gov.au/info/news/2016/09/aus-statistics-on-medicines-2015>.
[30] Peter Olson and Louise Sheiner, *The Hutchins Centre Explains: Prescription drug spending*, April 26, 2017 <https://www.brookings/edu>.
[31] See J Leighton, K Valverde and B Bernhardt, 'The general public's understanding and perception of direct-to-consumer genetic test results' (2012) 15 *Public Health Genomics* 11-21; Nick Bansback, Sonia Sizto, Daphne Guh and Aslam Anis, 'The effect of direct-to-consumer genetic tests on anticipated affect and health-seeking behaviours: A pilot survey' (2012) 16(10) *Genetic Testing and Molecular Biomarkers* <https://doi.org/10.1089/gtmb.2012.0074>; David Kaufman, Juli Bollinger, Rachel Dvoskin and Joan Scott, 'Risky business: Risk perception and the use of medical services among customers of DTCGT personal genetic testing' (2012) 21 *Journal of Genetic Counselling* 413-422.
[32] Additional manipulations were conducted testing the influence of lifestyle (Diabetes), family history (Cancer) and research confidence and dosage changes (Drugs) but these are not included in this thesis.

Scenarios contained only basic information to replicate the typically online receipt of the panel of test results and control potentially confounding variables. Experiments test whether particular independent variables affect particular dependent variables. Confounding variables are variables that might have a 'hidden' effect on dependent variables, essentially functioning as unanticipated additional independent variables. Removing extraneous information is one way to control for potential confounding variables.[33]

Two separate sets of scenarios were developed – one each employing male and female names commonly used in both countries. The scenarios were identical save for names and applicable pronouns. Use of names was done to foster identification with the named individual while allowing emotional distance from potentially confronting test results. This allowed individuals to 'project' their own responses onto others, especially useful for sensitive or personally confronting topics.[34] When answering psychological outcome and behavioural intention questions however, respondents were asked to assume test results were theirs.

*Disease predisposition: Determining the three risk levels to be used in experiments*

DTCGT disease predisposition tests provide information in percentage form on individuals' personal lifetime risk and the average person's lifetime risk derived from population studies. The average person's risk percentages for Type 2 Diabetes and Colorectal Cancer were taken from 23andMe sample test results: 20.7% and 4.0% respectively.[35] These were provided with 4 stars in the company's rating system, indicating general acceptance in the scientific community. These percentages also provided an interesting additional contrast between comparatively high and comparatively low average risks.

The aim in establishing the three levels of personal lifetime risk to be tested was to determine percentages not so obviously higher or lower as to lead while still generating sufficient response differentiation. A convenience sample of law students, academics and administration staff were presented with the average person's lifetime risk followed by a randomised list of numbers representing +/- 5%, 10%, 15%, 20%, 25% and 50% and + 75%, 100%, 125% and 150% of the average lifetime risk. Separate experiments were conducted by disease, each following the same format. Participation was voluntary and conducted in the researcher's absence with results

[33] See Andrea Skelly, Joseph Dettori and Erika Brodt, 'Assessing bias: the importance of considering confounding' (2012) 3(1) *Evidence-Based Spine-Care Journal* 9-12.
[34] See Lawrence Frank, 'Projective methods for the study of personality' (1939) 8, *The Journal of Psychology* 389-411.
[35] Company's 7 November 2013 website accessed through Web archive Wayback Machine (http://web.archive.org/web/20131107064641/https://www.23andme.com/health/all/).

presented in a lecture on big data. All respondents complete the exercise for both diseases with data from 31 respondents analysed, representing 6 females and 9 males under age 40 and 9 females and 7 males over 40. Analysis suggested +/- 20% and + 100% of average lifetime risk generated sufficient response differentiation. Further it indicated lower and much lower could be collapsed and 'about the same' should be added.

For this research, the three risk treatments are referred to as *Actual severity* with individual treatments labelled as AS(Low) representing average risk – 20%, AS(High) representing average risk + 20% and AS(Higher) representing average risk +100%. AS(Low) and AS(High) tested interpretation accuracy while AS(Higher) additionally tests the effect of quantum of disease risk. Respondents' personal risk interpretation is referred to as *Perceived severity* with individual interpretations labelled as PS(Lower), PS(Higher), PS(Same) and PS(Not sure). The latter was provided for respondents who felt unable to interpret results.

*Drug sensitivity: Determining metabolisation rate*

While 23andMe uses a variety of classification terms or types, it was decided to use 'Slow/fast metaboliser'. Metabolisation rate is one aspect that can have a significant impact if dosage is altered. For some drugs, slow metabolisers who self-increase risk potential overdose, while fast metabolisers who self-decrease risk reduced drug efficacy. Further, dosage levels for particular drugs take into consideration patient specifics and existing medications so changes can have compounding effects. A convenience sample of ten individuals was asked the difference between slow and fast drug metabolisation and if it mattered. Many used the example of overall metabolisation and its influence on weight for guidance e.g. 'I have a fast metabolisation rate so I can eat more. Isn't it the same for drugs?' This suggested the potential for confusion, justifying use of the terms.

#### *5.2.1.4 Sample scenarios*

Results were colour coded in the online survey to differentiate the three scenarios for respondents. Scenarios were repeated on each new screen within each experiment as a memory prompt. Figures 5.1, 5.2 and 5.3 provide examples of the randomised gender-specific scenarios.

*Type 2 Diabetes test results*

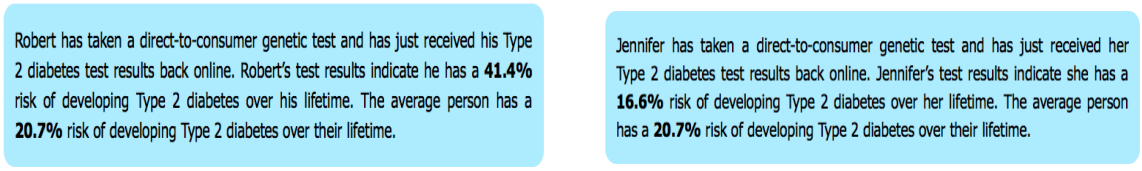


**Figure 5.1 Scenarios for males randomly allocated AS(Higher) and females randomly allocated AS(Low).**

*Colorectal Cancer test results*

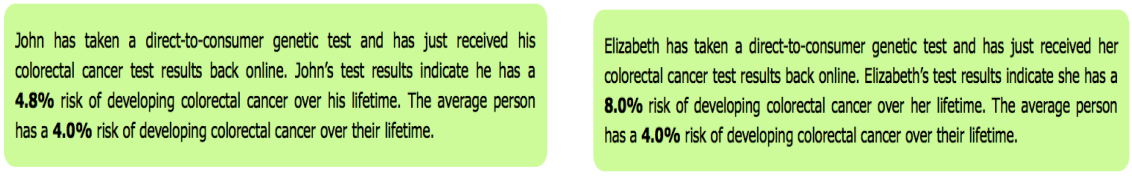


**Figure 5.2 Scenarios for males randomly allocated AS(High) and females randomly allocated AS(Higher).**

*Drug sensitivity test results*

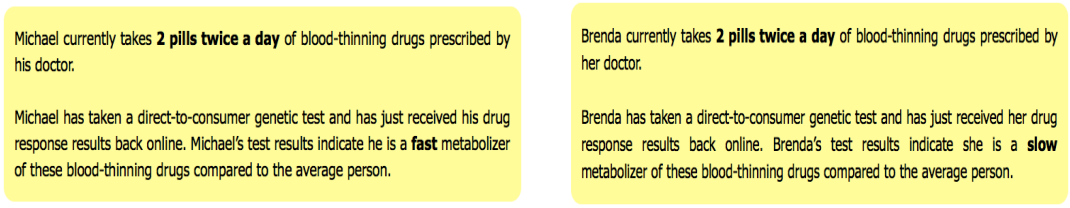


**Figure 5.3 Scenarios for males randomly allocated Fast and females randomly allocated Slow (US version).**

### *5.2.1.5 Scenario – directed questions*

For each of the three scenarios, respondents were first asked how easy they found results to understand. Self-report understanding provided insight into the context within which results would be interpreted and an indication as to confidence in their own interpretation. For diabetes and cancer, respondents were also asked about whether there was anything the named individual could do to prevent developing the disease (prevention attitude). Respondents were then asked to interpret the named individual's test results, comparing the average person's lifetime risk with the personal risk percentage randomly allocated.

#### 5.2.1.5.1 Testing the potential for psychological detriment

Emotions represent a form of consumer detriment in their own right as well as operating as precursors for longer-term psychological detriment.[36] For each of the three scenarios, core questions asked respondents to indicate how they would feel if their personal results were the same as the named individual's. Ten psychological outcome variables were tested: *anxious*, *upset*, *guilty*, *relieved*, *scared*, *nervous*, *stressed, concerned*, *interested* and *worried*. The affect or emotional states selected were based on the established Positive and Negative Affect Scale (PANAS) and concerns widely expressed about potential psychological harm.[37]

#### 5.2.1.5.2 Measuring behavioural intentions

Of interest was whether risk interpretation for disease predisposition scenarios and psychological outcomes for the three scenarios influenced behavioural intentions. For each scenario, respondents were asked to indicate what they might do, determining whether results and interpretation motivate behavioural change.

##### *Disease predisposition results*

For both diabetes and cancer, one general behavioural intention variable was tested – the intention to make no decisions. Thirteen specific behavioural intention variables were tested covering four key themes identified in the literature and modelling: lifestyle change, engagement with healthcare professionals, sharing, and information gathering. Three variables tested lifestyle change − changing diet, changing exercise and monitoring health.[38] Four variables tested engagement with healthcare professionals – visiting doctors for interpretation, confirmation of results, by special appointment and consulting genetic counsellors.[39] Three variables tested

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[36] Peter Lunt, Laura Miller, Johanna Körting and Joseph Ungemak, *The psychology of consumer detriment: A conceptual review* (2016) OFT792, Office of Fair Trading, United Kingdom <https://eprints.soton.ac.uk/148227/1/The_Psychology_of_Consumer_Detriment.pdf>.

[37] See David Watson, Lee Anna Clark & Auke Tellegan, 'Development and validation of brief measures of positive and negative affect: The PANAS scales', (1988) 54 (6), *Journal of Personality and Social Psychology* 1063-1070. See also John Crawford and Julie Henry 'The Positive and Negative Affect Schedule (PANAS): Construct validity, measurement properties and normative data in a large non-clinical sample', (2004) 43 *British Journal of Clinical Psychology* 245-265.

[38] See Dalva Nielsen, Deanna Carere, Catharine Wang, Scott Roberts and Robert Green, 'Diet and exercise change following direct-to-consumer personal genomic testing' (2017) 10(24) *BMC Medical Genomics* DOI: 10.1186/s12920-017-0258-1; Tinsley Webster, Sarah Beal and Kyle Brothers, 'Motivation in the age of genomics: why genetic findings of disease susceptibility might not motivate behavior change' (2013) 9(8) *Life Sciences, Society and Policy* <http://www.lsspjournal.com/contents/9/1/8>.

[39] See Burcu Darst, Lisa Madlensky, Nicholas Schork, Eric Topol and Cinnamon Bloss, 'Characteristics of genomic test consumers who spontaneously share results with their health care providers' (2014) 29(1) *Health Communication* DOI: 10.1080/10410236.21012.717216.

sharing intentions – with family, friends and online.[40] Respondents were also asked their intention to go online for information, to find others with similar results, and whether they would go online instead of visiting doctors.[41]

#### *Drug sensitivity results*

For drug sensitivity, respondents were asked their intention to make no decisions generally based on results. One specific behavioural intention variable was tested assessing whether individuals would alter medication regimes without medical consultation. Three independent decisions were tested − increase medication, decrease medication, and not change medication. One expert decision was tested − consult with doctor.

### *5.2.3 Pre and post-scenario questions*

To determine response variation by respondent, three suites of questions were asked to assess whether respondent characteristics, knowledge, attitudes and behaviours influenced engagement with results, generated differential vulnerability to psychological detriment, or affected purchase likelihood. It is acknowledged characteristics not studied may be more influential or may, in combination with characteristics studied, negate, diminish or intensify any influence found.

#### *5.2.3.1 Personal and health-related context*

##### *Personal characteristics and health status*

To determine if responses varied by personal characteristics, a standard suite of demographic questions was included: gender, age, education, income, marital status, children, employment and ethnicity. Respondents were gender and age qualified, with quotas established to ensure overall samples were gender and age representative of AU and US populations aged 18+.[42]

To determine if responses varied by personal health status, respondents were asked to self-assess health, lifestyle, indicate if taking prescriptions drugs, and family history of each of the two

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[40] See Kelly Stewart, Anke Wesselius, Maartje Schreurs, Annemie Schols and Maurice Zeegers, 'Behavioural changes, sharing behaviour and psychological responses after receiving direct-to-consumer genetic test results: a systematic review and meta-analysis' (2018) (9) 1-18; Tobias Haeusermann, Bastian Greshake, Alessandro Blasimme, Darja Irdam, Martin Richards and Effy Vayena, 'Open sharing of genomic data: Who does it and why?' (2017) *PLOS ONE* <https://doi.org/10.1371/journal.pone.0177158>.

[41] See Brent Rollins, Shravanan Ramakrishan and Matthew Perri, 'Direct-to-consumer advertising of predictive genetic tests: A health belief model based upon examination of consumer response' (2014) 31(3) *Health Marketing Quarterly* 263-278.

[42] Ethics approval obtained for individuals 18+ as they can sign contracts without parental consent in AU and US.

diseases.[43] Lifestyle and family history are known risk factors for both Type 2 Diabetes and Colorectal Cancer.[44]

### *Health-related skills, attitudes and behaviours*

#### Health-related skills

To determine if numeracy affected responses, in particular interpretation, two questions were asked – *risk numeracy* and *pills numeracy*.[45] While providing a general indication only, they are directly applicable to the sample DTCGT results presented.

#### Health-related attitudes

Respondents were asked a suite of questions concerning health-related attitudes around the key themes of health consciousness, health fatalism and causation specific to diabetes and cancer. Health consciousness and health fatalism represented the general context within which respondents interpret and engage with DTCGT results with causation the specific context for the two diseases. Four measures of health consciousness were tested – alert to changes, worry only when sick, responsible for health, and health depends on self-care. Three measures of health fatalism were tested – can control genetic risk, cannot prevent illness and cannot control genetic risk. These measures also provided insight into genetic literacy. Four causation questions tested the perceived importance of both family history and lifestyle to development of the two diseases.

To determine whether trust was related to past behaviours or might influence behavioural intentions, respondents were asked to indicate how much they trusted doctors, family, friends, the Internet and health-related online communities as sources of health information.

#### Health-related behaviours

To assess whether responses varied by selected health and online behaviours, respondents were asked the frequency with which they looked for health information online, used the Internet to self-diagnose, shared health-related or genetic information in online communities, and talked to their family about health issues in the past 12 months. These questions allowed for comparisons between behavioural intent relative to the sample DTCGT test results and actual behaviour.

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[43] See 'Self-assessed health status' in the report <http://www.abs.gov.au/ausstats/abs@.nsf/mf/4364.0.55.001>. The lifestyle variable reflects a combination of responses to diet and exercise questions.

[44] See <https://www.diabetesaustralia.com.au/type-2-diabetes> and <https://www.cancer.org/cancer/colon-rectal-cancer/causes-risks-prevention/risk-factors.html>.

[45] Risk numeracy refers to the ability to determine and differentiate between levels of risk. Pills numeracy refers to the numerical skills needed to self-manage medications.

### 5.2.3.2 DTCGT-related context

#### DTCGT-related knowledge

Respondents were asked at the outset how familiar they were and whether they had purchased DTC tests. While these questions did not specify health-related tests, given the preamble it is reasonable to expect respondents were in a health-related mindset. Those who had purchase experience would be familiar with providing DNA samples and self-interpreting/actioning results. While past behaviour does not guarantee future behaviour, it is can be used to predict future behaviour and, considered with familiarity, was used to verify sample proportions of early adopters and non-early adopters.[46]

#### DTCGT-related attitudes

Confidence is 'the degree of certainty that one's evaluative judgement of the brand is correct'[47] and is one of the key determinants of purchase intentions.[48] After engagement with sample results, respondents were asked their level of confidence in the DTCGT offering. Four confidence measures were tested − accuracy of DTCGT results, completeness of information to inform decisions, personal ability to interpret genetic test results, and genetic information shared only with permission.[49] The four measures were also combined into an overall confidence measure. These variables allowed testing to determine if confidence affected purchase likelihood and willingness to participate in DTCGT research.

#### DTCGT- related behavioural intentions

Two behavioural intentions were measured: purchase likelihood and willingness to participate in DTCGT research. Exposure to potential psychological detriment and possessing genetic data for sharing is dependent on whether consumers purchase tests. Purchase likelihood is a measure of behavioural intention so higher purchase likelihood should indicate higher potential exposure and possession of data. Purchase likelihood data also provides insight into consumer acceptance of

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[46] See Judith Oeullette and Wendy Wood, 'Habit and intention in everyday life: The multiple processes by which past behavior predicts future behaviour' (1999) 124(1) *Psychological Bulletin* 54-74.
[47] John Howard, *Consumer Behavior in Marketing Strategy* (Prentice Hall, 1989), 34.
[48] See Michel Laroche, Chankon Kim and Lianxi Zhou, 'Brand familiarity and confidence as determinants of purchase intention: An empirical test in a multiple brand context' (1996) 37 *Journal of Business Research* 115-120; P Bennett and G Harrell, 'The role of confidence in understanding and predicting buyers' attitudes and purchase intentions' (1975) 2 *Journal of Consumer Research* 110-117.
[49] See Andelka Phillips and Jan Charbonneau, 'Giving away more than your genome sequence?: Privacy in the direct-to-consumer genetic testing space'(2016) presentation at the Federal Trade Commission's Privacy Con, Washington, DC <https://www.ftc.gov/system/files/documents/public_comments/2015/10/00057-98101.pdf>.

different business models. This is important information for companies operating in or planning to enter as well as regulators seeking to protect consumers in the DTCGT space.

One major concern has been the Internet's jurisdictional and enforcement challenges as increasing numbers of consumers purchase offshore and online, especially if tests are unavailable onshore. Company location has legal implications as it dictates applicable contract and consumer protection law, ability to enforce judgments and regulatory bodies with authority. Before exposure to scenarios, purchase likelihood was tested for purchase from an onshore and again for an offshore company.[50]

As discussed in Chapter Four, concern has been expressed broadly about the absence of professional interpretation and counselling in the DTCGT offering. Modelling of the DTCGT space in Chapter Three revealed an increasing number of DTCGT companies engaging with consumers directly pre-sale through to sample provision but returning results via healthcare professionals or affiliates. After exposure to scenarios, purchase likelihood was tested for results returned via doctor option.

Respondents were provided with DTCGT test information at the outset so all were judged to have reasonable familiarity to respond to the onshore/offshore options, regardless of actual familiarity. Responses for the results via doctor option can be considered as an informed response as all respondents had already experienced engaging with three sets of sample results.

Respondent willingness to participate in DTCGT research was tested in three situations to determine whether who would use their data influenced willingness to participate. DTCGT companies have a history of collaborating with academic and non-profit researchers so one situation was if the information was provided at no cost to researchers in colleges or universities. As DTCGT contracts generally include no benefit-sharing clauses, an 'altruistic' motivation was tested. The third tested willingness to participate if personal information would be sold for profit to another company for their research.

[50] See Gordana Bruce and Christine Critchley (2013) *Swinburne National Technology and Science Monitor* <http://apo.org.au/system/files/119126/apo-nid119126-477751.pdf>. Purchase likelihood questions by Jan Charbonneau.

### 5.2.4 Pre-testing the survey instrument and survey schematic

#### 5.2.4.1 Pre-testing the survey instrument

Pre-testing of the draft survey instrument was conducted to minimise errors, gauge how questions were interpreted and determine completion time, allowing for re-crafting before survey fielding. The pre-test was conducted in February 2015 using hardcopy survey instruments with respondents provided gender-specific versions with randomised allocation of scenarios. Participation was voluntary and survey completion was in the researcher's absence. A convenience sample of law students, academics and administration staff generated 26 completed surveys. This represented 7 females and 4 males under the age of 40 and 8 females and 7 males over 40, none of whom had participated in the risk percentage exercise.

Debriefing of respondents confirmed the initial information on DTCGT provided sufficient context and identified slight changes required and questions deemed sensitive. For example, the phrase ‘inside your country’ was changed to ‘inside your country of residence’, with 'prefer not answer' option included for all sensitive questions. All finished within 20 minutes and reported survey instructions, scenarios and general questions easy to understand.

#### 5.2.4.2 Survey schematic

Figure 5.4 provides a schematic of the survey illustrating survey flow and should be read in conjunction with the annotated sample survey provided in Appendix Two.

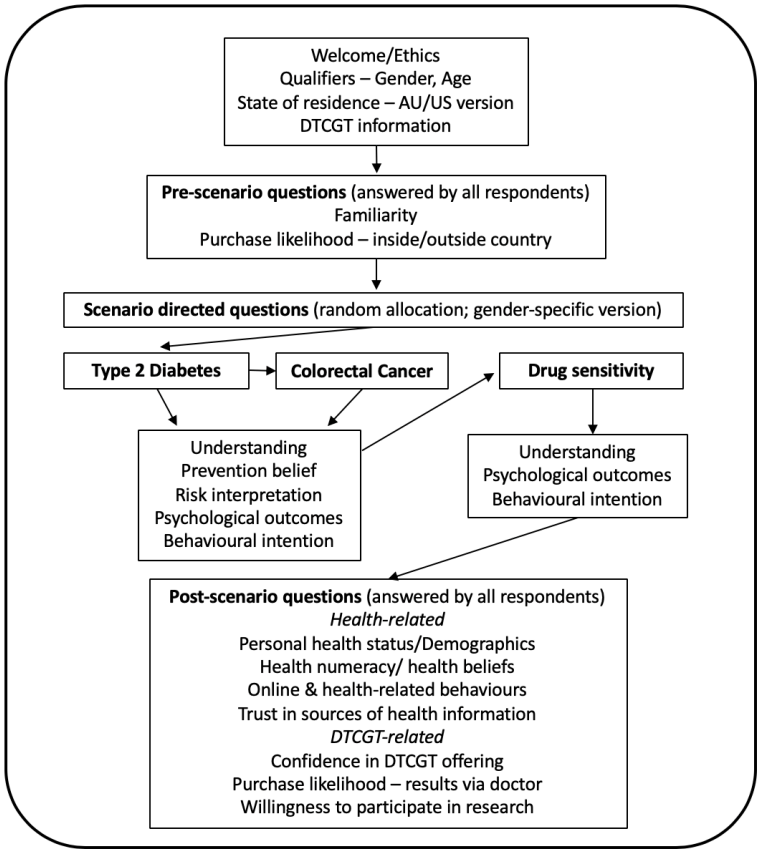


**Figure 5.4 Survey schematic**

## PART THREE: METHODS SELECTION – HOW TO TEST?

All research methods have both benefits and limitations and are best suited to achieve different research objectives.[51] The aim here was to select the research method best suited to this study's particular research objectives. As the majority of DTCGT companies operate entirely or partially online and typically return results online, potential customers need to be Internet-literate. The most efficient way to access respondents in the two countries meeting this criteria was an online survey using an online panel to control for gender and age representativeness. Online research is now well established in both corporate and academic research and represents a significant proportion of research conducted globally. Of the US$68 billion spent in 2016, US$28 billion (41%) was online with growth expected to continue.[52]

[51] See André Queirós, Daniel Faria and Fernando Almeida, 'Strengths and limitations of qualitative and quantitative research methods' (2017) 3(9) *European Journal of Education Studies* 369-387.
[52] ESOMAR, 'Global Market Research 2016', <https://www.esomar.org/uploads/public/publications-store/reports/global-market-research-2016/ESOMAR-GMR2016_Preview.pdf>. See also George Terhanian and John Bremer, 'A smarter way to select respondents for surveys' (2012) 54(6) *International Journal of Market Research* 751-780.

Gathering data online is inherently biased against non-Internet users, generating questions about representativeness.[53] However, as Internet-literate individuals are the primary target consumers for DTCGT companies, and therefore this research, it was appropriate to assess their engagement with DTCGT rather than non-users. Given Internet penetration is high in both countries with 88% of Australians and a comparable number of Americans active online, representativeness was not overly compromised.[54]

### 5.3.1 Online panels: Benefits and limitations

Online panels are now a prominent way to collect market, social, psychological, political and medical research data and are increasingly being used in academia.[55] Online panels are a form of access panels, defined as 'a sample database of potential respondents who declare that they will cooperate for future data collection if selected'.[56] As with all research methods, online panels have both benefits and limitations.[57]

#### 5.3.1.1 Benefits of online panels

Online surveys offer functionality such as randomisation, validation, automatic branching, qualifiers and quotas. Randomisation of questions and answer options assists in ensuring careful reading and overcoming order effects – the differences in participants' responses and potential bias that result from the order in which the experimental materials are presented.[58] The one exception is options such as 'not sure', which are generally presented last.

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[53] See Gian Fulgoni, 'Numbers, please: Uses and misuses of online-survey panels in digital research' (2014) 54(2) *Journal of Advertising Research* 133-137.

[54] 'Active Internet users as a percentage of the total population in Australia from 2015 to 2018' <www.statista.com/statistics/680142/Australia-internet-penetration>; 'Share of adults in the United States who use the Internet in 2018, by gender' <https://www.statista.com/statistics/327130/internet-penetration-usa-gender/>.

[55] See Reg Baker, Stephen Blumberg, Michael Brick, Mick Couper, Melanie Courtright, Michael Dennis, Don Dillman, Martin Frankel, Philip Garland, Robert Groves, Courtney Kennedy, Jon Krosnick, Paul Lavrakas, Sunghee Lee, Michael Link, Linda Piekarski, Kumar Rao, Randall Thomas and Dan Zahs, 'AAPOR Report on online panels' (2010) 74(4) *Public Opinion Quarterly* 711-781.

[56] ISO 20252 'Market, opinion and social research – Vocabulary and Service Requirements' – see Mario Callegaro, Reg Baker, Jelke Bethlehem, Anja Goritz, Jon Krosnick and Paul Lavrakas (eds), *Online panel research: Data Quality Perspective* (John Wiley & Sons, 2014).

[57] See Janet Ilieva, Steve Baron and Nigel Healey, 'Online surveys in marketing research: pros and cons' (2002) 44(3) *International Journal of Market Research* 361-376; Ronald Fricker and Matthias Schonlau 'Advantages and disadvantages of Internet research surveys: Evidence from the literature' (2002) 14(4) *Field Methods* 347-367.

[58] See Fritz Strack, 'Order effects in survey research: Activation and information functions of preceding questions' in Norbert Schwartz and Seymour Sudman (eds), *Context Effects in Social and Psychological Research* (Springer-Verlag, 1992) 23-44.

Nonresponse at overall survey and individual question levels represents a significant problem in survey research. With online panels, respondent numbers and qualifications are contracted at the outset overcoming overall nonresponse. Validations eliminate item non-response − the situation when specific questions or aspects are missed requiring researchers to use statistical estimations and manipulations to 'fill in' missing data.[59] Validations require respondents to fully answer before advancing and are a common feature in online research. Respondents who are uncomfortable with validations, indeed any aspect of the survey, always have the option to terminate without prejudice.

Automatic branching directs respondents to particular questions based on responses to preceding questions. Qualifiers ensure respondents with particular characteristics in desired proportions are included in the sample. Quotas can be combined with randomisation and branching to ensure equal proportions are exposed to particular experiment treatments. Further, automatic uploading of responses into statistical analysis software reduces data entry errors.

With an online panel, '… costs of locating potential respondents can be substantially reduced and clients of online panels benefit from the immediate availability of large samples with various key characteristics and shorter field times.'[60] It has been suggested that 'internet surveys are 5 to 15 times less expensive than comparable phone surveys and over 50 times less expensive than face-to-face'.[61]

### *5.3.2 Limitations of online panels*

#### *Non-probability sampling*

It has been suggested no sampling strategy is inappropriate per se but must instead be empirically or theoretically justified.[62] Ensuring samples are representative of general or specific populations

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[59] See Jean Phillippe Décieux, Alexandra Mergener, Kritina Marliese Neufang and Phillipp Sischka, 'Implementation of the forced answering option within online surveys: Do higher item response rates come at the expense of participation and answer quality?' (2015) 48(4) *Psihologija* 311-326; Ting Yan and Richard Curtin, 'The relation between unit nonresponse and item nonresponse: A response continuum perspective', (2010) 22(4) *International Journal of Public Opinion Research* 535-551.

[60] Mario Callegaro, Reg Baker, Jelke Bethlehem, Anja Goritz, Jon Krosnick and Paul Lavrakas (eds), *Online panel research: Data Quality Perspective* (John Wiley & Sons, 2014), 172.

[61] Charles Breton, Fred Cutler, Sarah Lachance and Alex Mierke-Zatwarnicki, 'Telephone versus online survey modes for election studies: Comparing Canadian public opinion and vote choice in the 2015 Federal Election' (2017) 50(4) *Canadian Journal of Political Science* 1005-1036, 1005.

[62] See Richard Landers and Tara Behrend, 'An inconvenient truth: Arbitrary distinctions between organisational, Mechanical Turk, and other convenience samples' (2015) 8(2) *Industrial and Organisational Psychology* 142-164; Nicolas Roulin, 'Don't throw the baby out with the bathwater: Comparing data quality of crowdsourcing, online panels and student samples' (2015) *Industrial and Organisational Psychology* DOI: 10.1017/iop.2015.24.

is always of concern, regardless of methods employed. Traditionally researchers have preferred probability samples where subjects have an equal and known possibility of being selected from the general population.[63] However, probability samples may not be either feasible or theoretically sensible when particular populations are the subject of enquiry. Depending on the survey specifics, 'the generally lower cost and unique properties of Web data collection are an acceptable alternative to traditional probability-based methods.'[64] Further analysis of government survey data now suggests probability and non-probability samples generate similar findings.[65]

Online panels generate non-probability samples as respondents are drawn from their particular self-selected membership, initially drawn from those with Internet access. Respondents self-select specific survey participation creating inherent self-selection bias however this is present in all surveys, regardless of delivery mode. Early research suggested online panels were disproportionately white, higher educated and more active Internet users.[66] However, as Internet penetration increases, there is a greater chance 'a panel may reflect the socio-demographic characteristics of the entire population.'[67]

In response to early concerns, online panel providers now generally partner with other panel providers to allow access to larger, diverse or targeted populations and have the functionality to offer quota sampling. Quota sampling involves surveying relevant proportions in subclasses or

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[63] See E Bruggen, J van den Brakel and J Krosnick 'Establishing the accuracy of online panels for survey research' (2016) Discussion paper 04, Statistics Netherlands; David Yeager, Jon Krosnick, Linchiat Chang, Harold Javitz, Matthew Levendusky, Albert Simpser and Rui Wang, 'Comparing the accuracy of RDD telephone surveys and Internet surveys conducted with probability and non-probability samples' (2011) 75(4) *Public Opinion Quarterly* 709-747.

[64] Reg Baker, Stephen Blumberg, Michael Brick, Mick Couper, Melanie Courtright, Michael Dennis, Don Dillman, Martin Frankel, Philip Garland, Robert Groves, Courtney Kennedy, Jon Krosnick, Paul Lavrakas, Sunghee Lee, Michael Link, Linda Piekarski, Kumar Rao, Randall Thomas and Dan Zahs, 'AAPOR Report on online panels' (2010) 74(4) *Public Opinion Quarterly* 711-781, 713, 714.

[65] John Boyle, Ronaldo Iachan, Naomi Freedner-Maquire and Tala Fakhouri, 'Characteristics of the population of Internet panel members' (2017) 10(4) *Survey Practice* 1-9.

[66] Reg Baker, Stephen Blumberg, Michael Brick, Mick Couper, Melanie Courtright, Michael Dennis, Don Dillman, Martin Frankel, Philip Garland, Robert Groves, Courtney Kennedy, Jon Krosnick, Paul Lavrakas, Sunghee Lee, Michael Link, Linda Piekarski, Kumar Rao, Randall Thomas and Dan Zahs, 'AAPOR Report on online panels' (2010) 74(4) *Public Opinion Quarterly* 711-781; John Boyle, Ronaldo Iachan, Naomi Freedner-Maquire and Tala Fakhouri, 'Characteristics of the population of Internet panel members' (2017) 10(4) *Survey Practice* 1-9, 2.

[67] Mario Callegaro, Reg Baker, Jelke Bethlehem, Anja Goritz, Jon Krosnick and Paul Lavrakas (eds), *Online panel research: Data Quality Perspective* (John Wiley & Sons, 2014), 2; Miliaikeala Heen, Joel Liberman and Terrence Miethe, 'A comparison of different online sampling approaches for generating national samples' (2014) *Research in Brief University of Nevada Centre for Crime and Justice Policy* 1-7.

strata of populations of interest and is now the most commonly used sample selection method.[68] Qualifiers and quotas ensure samples have the same proportions on key criterion such as demographics as dictated by researchers. It has been suggested that 'we may have reached a point where internet surveys using commercial panels will satisfy the needs of academic researchers at least as well as telephone surveys'.[69]

### *Respondents*

Individuals join panels for a variety of reasons, such as having their opinions heard and incentives offered.[70] Incentives are commonly used in survey research to increase response rates.[71] Online panels generally offer post-paid incentives for successful provision of quality responses, redeemed via conversion to cash or gift cards and calculated based on length of survey.

It has been suggested 'professional respondents' such as members of multiple panels affect data quality through satisficing, speeding and straightlining. Satisficing includes behaviour such as always selecting 'not sure'; speeding answering without careful consideration; and straightlining always selecting the same answer option regardless of question. However, there has been no consistent evidence suggesting 'professional respondents' engage in these behaviours any more than other respondents.[72] Researchers guard against these behaviours through survey design such as reversing scales and pre-testing. The industry has responded to these concerns by instituting strict quality control measures, screening out dishonest, inaccurate and speedy respondents.

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[68] Mario Callegaro, Reg Baker, Jelke Bethlehem, Anja Goritz, Jon Krosnick and Paul Lavrakas (eds), *Online panel research: Data Quality Perspective* (John Wiley & Sons, 2014), 12. With quota sampling, respondents are selected to reflect proportions in the various subclasses (or strata) of the population of interest.

[69] Charles Breton, Fred Cutler, Sarah Lachance and Alex Mierke-Zatwarnicki, 'Telephone versus online survey modes for election studies: Comparing Canadian public opinion and vote choice in the 2015 Federal Election' (2017) 50(4) *Canadian Journal of Political Science* 1005-1036, 1005. See also Stephen Ansolabehere and Brian Schaffner, 'Does survey mode still matter? Findings from a 2010 multi-mode comparison' (2014) 22 *Political Analysis* 285-303; Josh Pasek, 'When will nonprobability surveys mirror probability surveys? Considering types of inference and weighting strategies as criteria for correspondence' (2016) 28 *International Journal of Public Opinion Research* 269-291.

[70] Mario Callegaro, Reg Baker, Jelke Bethlehem, Anja Goritz, Jon Krosnick and Paul Lavrakas (eds), *Online panel research: Data Quality Perspective* (John Wiley & Sons, 2014), Chapter 8.

[71] Mike Brennan and Jan Charbonneau, 'Improving Mail Survey Response Rates Using Chocolate And Replacement Questionnaires' (2009) 73(2) *Public Opinion Quarterly* 368-378.

[72] Healey Whitsett 'Understanding "Frequent survey responders on online panels', 1 April 2013, *Insight into Economics* Nera Economic Consulting <http://www.nera.com/content/dam/nera/publications/archive2/PUB_Frequent_Survey_Responders_0313.pdf>.

While the limitations of online research, online panels and suggested difference between online and offline respondents are acknowledged, the benefits outweighed limitations relative to this particular research given its need for Internet-literate respondents and functionality to execute the experimental design.

### *5.3.2 Qualtrics: Online panel provider*

Qualtrics was selected as survey host and respondent provider. Qualtrics is a major international provider for corporate, governmental and academic research, having worked with the Australian Tax Office amongst others.[73] Qualtrics was able to provide access to respondents in multiple countries through its partner international panel providers, stringent quality control features and the platform functionality such as quotas and quotas needed to conduct the experiments. Qualtrics adheres to all ISO standard and industry standard data protection and security procedures and employs quality control measures such sophisticated digital fingerprinting technology to exclude duplication and participation limits to ensure respondents are not oversampled.

Qualtrics adheres to the ICC/ESOMAR International Code on Market and Social Research in all recruitment and survey hosting activities, with all partner providers also ESOMAR members. With membership from 130 countries, ESOMAR is considered the peak international body for public opinion and market research. This Code sets out ethical rules and has been endorsed by over 60 national market research associations and peak bodies such as the American Association of Public Opinion Research, the World Association of Public Opinion Research and the Australian Market and Social Research Society. Qualtrics also adheres to the Codes of Ethics of the American Marketing Association and the Market Research Association.

Qualtrics has an office in Sydney, is familiar with Australia's NHMRC *Statement on Ethical Conduct in Human Research*, and did not require separate in-country ethics approvals to be sought for the American respondents. The survey included the ethics statement required as a condition of Ethics approval (Human Research Ethics Committee (Tasmania) network, Social Sciences HREC approval H0013321).[74] The researcher was removed from actual data collection although could monitor

[73] See Brent Rollins, Shravanan Ramakrishnan and Matthew Perri 'Direct-to-consumer advertising of predictive genetic tests: A health belief model based on examination of consumer response' (2014) 31(3) *Health Marketing Quarterly* 263-278 for an example of academic research using Qualtrics.
[74] Australian Government, NHMRC, National Statement on Ethical Conduct in Human Research (2007) (updated 2018).

key statistics such as female completions, and was only provided with de-identified data, removing any possibility of respondent identification.

# PART FOUR: DATA COLLECTION AND ANALYSIS

## *5.4.1 Data collection: Fielding the survey*

The survey was uploaded into the Qualtrics template and quotas established for gender and age group and scenario allocation. Validations ensured full data was obtained and care was taken to provide 'prefer not to answer' and 'not sure' options for those who were uncertain or uncomfortable answering sensitive questions such as income. Branching allowed respondent allocation into appropriate country and gender surveys. The maximum number of questions per screen and design was revised several times to achieve the desired look and flow.

As per Qualtrics standard procedure, a soft launch was conducted on 19 March 2015 where data was collected from 104 AU and 101 US respondents and the survey paused. The purpose of the soft launch was two-fold, firstly to establish the median time for completion, and secondly to ensure all functionality such as randomisation and quotas was working. The median time was used to calculate the cut-off point under which respondents were judged to have completed the survey too fast for informed answers, requiring replacement. The median time for AU respondents was 15 minutes and 14 minutes for US respondents. While the industry standard is to set the cut-off at one-third of the median time, given the experimentation was quite complex, a cut-off of 10 minutes (⅔) was used.

The survey was launched on 22 March and closed on 27 March 2015 with data provided from Qualtrics on 28 March in SPSS format. After all data was fully reviewed, quotas and random allocations verified and the 10 minute cut-off for respondent data removal strictly applied, data from AU and US respondents was put through a cleaning script before the two data sets were merged. As the uploaded survey contained all versions of each of the scenarios with respondent data only recorded for each respondent's random allocation, the cleaning script eliminated all extra scenario versions.

Table 5.1 outlines the percentage and number of respondents allocated into each level of risk for diabetes and cancer and each metabolisation rate for drug sensitivity. Review verifies the random allocation quotas were effective at ensuring equal samples for each random allocation category.

**Table 5.1 Random allocation: Percentage and participant numbers (AU & US)**

| Random allocation | Country | |
|---|---|---|
| % (# respondents) | AU | US |
| *Type 2 Diabetes* | | |
| Low risk | 33.1 (331) | 33.4 (334) |
| High risk | 33.4 (334) | 33.1 (331) |
| Higher risk | 33.5 (335) | 33.5 (335) |
| *Colorectal Cancer* | | |
| Low risk | 33.6 (336) | 33.2 (332) |
| High risk | 33.5 (335) | 33.4 (334) |
| Higher risk | 32.9 (329) | 33.4 (334) |
| *Drug sensitivity* | | |
| Slow metaboliser | 49.9 (499) | 49.8 (498) |
| Fast metaboliser | 50.1 (501) | 50.2 (502) |

### 5.4.2 Data analysis

After data collection, cleaning and coding, preliminary data analysis was conducted to get an overview of the data. All data analysis was conducted using the Statistical Package for the Social Sciences (SPSS) software version 24. Variables were reverse coded as appropriate, recoded, new variables created and data reduction techniques conducted before full-scale analysis. As this research was exploratory in nature, data analysis was an iterative process, with recoding, creation of new variables and data reduction continuing throughout.

### 5.4.3 Statistical tests

A range of statistical analyses were conducted with specific statistical tests dictated by research questions, variable type (questions) and scales used (answer options). Appendix Three explains tests conducted, determination of statistical significance, calculation of residuals and effect sizes, and interpretation of correlations. Appendix Four provides details of Exploratory and Confirmatory Factor Analysis, the data reduction technique conducted to reduce psychological outcome, behavioural intention and health attitude variables into composite measures.

A variety of variables were used as appropriate for the research question. Variables are 'any characteristics, number or quantity that can be measured or counted' and are broadly categorised as numeric or categorical.[75] Numeric variables describe measurable quantities as numbers and are

[75] Australian Bureau of Statistics, 'Statistical language – What are variables?' <http://www.abs.gov.au/websitedbs/a3121120.nsf/home/statistical+language+-+what+are+variables>.

either discrete (whole numbers) or continuous (fractions). Categorical variables describe measurable quantities as one of a fixed number of mutually exclusive values. Categorical variables are either nominal, representing values that cannot be organised in logical sequences (e.g. males, female) or ordinal, representing values that can be logically ordered (e.g. low, high, higher).

When conducting analysis or running experiments, variables are treated as either independent or dependent. Independent variables (IV) are thought to lead to, or predict, particular outcomes while dependent variables (DV) are the outcomes. In an experiment, the IV is changed or manipulated to test its effect on the DV: does a change in the IV produce a statistically significant change in the DV?

Scales used were dependent on variable type with nominal scales used for discrete and nominal variables where numbers served simply as labels such as 1 = male. Likert-type and other scales were used for continuous and ordinal variables. Likert scales are one of the most commonly used rating scales and assume linearity on a continuum such as strongly disagree to strongly agree.[76] These scales however are arbitrary as values assigned to each point have no objective numerical basis e.g. strongly agree is arbitrarily assigned a value of 5.

Scales were generally treated as interval scales with equal degrees of difference assumed between each answer option. Semantic differential scales with dichotomous anchors at either end were used to measure psychological outcomes e.g. not worried/worried.

Univariate, bivariate and multivariate inferential statistical tests were conducted. Univariate tests describe or summarise one variable while bivariate tests determine relationships or associations between two variables. Multivariate tests are more complex and are conducted when there is more than one outcome or dependent variable.[77] These tests were used to determine differences between specific groups (chi-square, T-test, ANOVA and MANOVA analysis), relationships between variables (Exploratory and Confirmatory factor analysis and correlations) and predict respondent membership in particular groups (multinomial logistic regression).

## PART FIVE: INTERPRETATION RULES

The following interpretation rules were applied to all statistical analysis generating the results presented in Chapter Six. The priority for this research was to identify broad patterns and

[76] See Rensis Likert, 'A technique for the measurement of attitudes' (1932) 22 *Archives of Psychology* 1-55.
[77] See Barbara Tabachnick and Linda Fidell, *Using Multivariate Statistics* 6e (Pearson, 2014).

consistency within or between countries, type of test and respondents to generate meaningful and actionable regulatory insight. It was felt focusing on consistent, robust, conservatively determined patterns would provide more insight to Australian regulators than detailed analysis identifying every difference between these two specific sets of respondents.

Given robust sample sizes and the exploratory nature of this analysis, a conservative approach was taken for interpretation. Determining sample size is always a balancing act between statistical power (finding an effect when one exists) and cost. The sample size of 1000 per country was judged to provide sufficient statistical power. While no overall rule of thumb for sample size exists, there are rules for different types of tests. For example, correlations need a minimum of 50 and chi-squares 20 with no cell smaller than 5. In all instances, rules of thumb for specific tests were met for this research.[78]

To avoid spurious findings due to the large sample size, the more rigorous cut-off point of $p \leq 0.001$ rather than $p < 0.05$ was used to determine statistical significance for Chi-squares, Adjusted residuals, T-tests and ANOVAs. As such, any discussion of non-significant results should be read as 'not significant at $p \leq 0.001$'. The exception to this was T-tests, ANOVA and MANOVA analysis using composite measures where two levels of statistical significance are discussed: $p \leq 0.001$ and $p > 0.001$ and $< 0.05$.

This conservative approach was taken to guard against Type I errors (false positives). However, strict adherence to these cut-off points may have generated Type II errors (false negatives), meaning some statistically significant results may have been missed.[79] Guarding against Type I errors was considered the priority to ensure that conclusions were not based on inaccurate determinations of significance, ensuring maximum confidence in results discussed. Care should, however, be taken when considering any results deemed to be not statistically significant as a result of this conservative approach as they may reflect Type II errors.

When analysing the results of Chi-square tests, only adjusted residuals that were 3.3 and greater are discussed as these represent differences that are statistically significant at the $p < 0.001$ level (*cf.* $1.98 - 3.28 = p < 0.05$). Given that strength, they are phrased as 'much *more* likely' for positive adjusted residuals and 'much *less* likely' for negative adjusted residuals in the analysis narrative.

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[78] See Cameron Wilson Van Voorhis and Betsy Morgan, 'Understanding power and rules of thumb for determining sample sizes' (2007) 3(2) *Tutorials in Quantitative Methods for Psychology*, 43-50; Alan Agresti, *An Introduction to Categorical Data Analysis* 2e (John Wiley & Sons, 2007.

[79] See Kenneth Rothman, 'Curbing type I and type II errors' (2010) 25 *Eur J Epidemiol* 223-224.

This phrasing should be read as 'much more/much less likely than would be expected by chance' in all instances.

In keeping with the conservative approach, Cohen's categories were used to determine effect sizes for all Phi and Cramer's V statistics in addition to their common application in correlations. Cohen suggests that any effect from 0.10 to 0.29 is small, 0.30 to 0.49 is moderate and 0.50 to 1.0 is strong.[80] To be conservative, only moderate and large effects were discussed for both effect size and correlations.

For the Multinomial logistic regression, statistical significance was determined at $p < .01$. This less stringent cut-off point was appropriate, as data is carved up by groups when multiple independent variables are used.

Full codes for all variables were used in Exploratory and Confirmatory factor analysis, Repeated measures ANOVAs, and correlations as required. All other analysis used recoded variables. Initial analysis using full codes revealed US respondents were much more likely to express stronger opinions (propensity to strongly agree/strongly disagree) compared to AU respondents (propensity to agree/disagree). This generated large numbers of mathematically derived statistically significant differences, especially means, that were not present when recodes considering overall levels of agreement or disagreement were analysed. Frequency analysis confirmed that AU and US respondents expressed comparable overall levels of agreement or disagreement, confirming the decision to use recodes to establish broad patterns.

## CONCLUSION

This chapter outlined the specific aims of the research, methods selected, how experiments were crafted and survey questions developed, and finally how the resulting data was analysed. As such it provides the context within which to consider the results discussed in Chapter Six. Of particular importance is the discussion of interpretation rules, as the conservative approach taken must be kept in mind when considering results presented in the next chapter.

The three areas of concern discussed in the preceding chapter were reflected in the survey instrument designed to provide the data required to answer the specific research questions outlined in Part One. Concerns about the DTCGT offering were tested with questions such as

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[80] See Jacob Cohen, *Statistical power analysis for the behavioural sciences* 2e (Lawrence Erlbaum Associates, 1988), 79-81.

confidence in DTCGT accuracy and purchase likelihood, providing data addressing *Research question 2*. Potential impact on individuals was tested with questions such as those on interpretation of sample test results, resulting affect and behavioural intentions such as prescription changes, providing data addressing *Research questions 1 and 3*. Concerns about the impact on the healthcare system were tested through specific behavioural intentions such as seeking professional assistance with interpretation, providing data addressing *Research question 4*. A broad range of questions were asked to determine response variation including personal characteristics and health status and health-related attitudes, providing data to address *Research question 5*. Taken together, the data collected provides the information necessary to identify the broad patterns and relationships relative to consumer engagement with DTCGT, the overarching aim of this component of the research.

*Acknowledgments*

Exploratory factor analysis was conducted by the researcher and confirmed by Professor Christine Critchley, who also conducted Confirmatory Factor analysis in consultation with the researcher. Jarrod Walshe, Swinburne University uploaded the survey into the Qualtrics template, developed the cleaning script, merged datasets and assisted with initial creation of merged variables.

# Chapter Six:

# Engaging with DTCGT: Does one size fit all?

*'We want to give information to individuals where there is no ambiguity.'*[1]

Anne Wojcicki, CEO 23andMe

[1] Kulrag Singh Bhangra, '23andMe halts development of next-generation gene sequencing', www.bionews.org/uk/page_719553.asp, 31 October 2016. Anne Wojcicki discussing the company's decision to halt next-generation sequencing with BuzzFeed News.

# INTRODUCTION

Consumer empowerment is about taking personal control over healthcare and can occur only when consumers contextualise, understand and interpret, experience justified levels of affect, and engage in behaviours consistent with their DTCGT results: one result, one meaning for all, no ambiguity. But what if there is ambiguity: one result, different meanings for different individuals? The experiments embedded in the survey component of this research were designed to find out if ambiguity does exist and, if so, what happens relative to how individuals would feel and what they might do in response to DTCGT results.

As with all survey research, results presented in this chapter represent a snapshot of a particular group of respondents at a particular time, and should be considered as indicative not definitive.[2] The survey also presented *potential* consumers with *hypothetical* DTCGT results, an acknowledged limitation. Survey results do however provide a baseline, providing insight into broad patterns and allowing subsequent charting of changes. As noted in Chapter One, the US is clearly a lead market, with Australia lagging behind relative to DTCGT uptake. As such, benchmarking Australian results against those from the US provides Australian regulators insight through a 'glimpse of the future', should DTCGT uptake increase as is forecasted.

Given such a robust dataset investigating large numbers of variables, even applying conservative interpretation rules, large numbers of statistically significant results were found, far more than could realistically be reported. Rather than delve into nuanced detail, no matter how tempting, this chapter instead focuses on identifying broad and consistent patterns inter-respondent, country and type of test, and relationships between variables. Insights gained from this approach were judged to be more valuable to regulators for determining whether existing regulation provides sufficient protection for DTCGT consumers.

This chapter is organised into five parts. Part One investigates the context within which DTCGT engagement occurs. Each consumer brings to DTCGT engagement their own personal characteristics and health status; existing health-related numeracy skills, attitudes towards healthcare and trust in various sources of health information; and existing health-related

[2] This chapter should be read in conjunction with Chapter Five: Part Five: Interpretation rules; Appendix Two: Annotated Sample Survey; Appendix Three: Statistical Tests Conducted; Appendix Four: Exploratory and Confirmatory Factor Analysis; and Appendix Five: MANOVA Analysis. To illustrate broad patterns, percentages are rounded to one decimal place and means to two decimals. Standard deviations, adjusted residuals, chi-square, T-test and ANOVA notations as well as more detailed statistical analysis is available on request. Only results meeting Chapter Five Interpretation rules are discussed so if, for example, no comment is made for AU there were no statistically significant differences found.

behaviour patterns such as use of the Internet for self-diagnosis or as a source of health information.

Part Two analyses results of the survey's experimental component to determine how consumers attach meaning to DTCGT results and the resulting affect experienced and behavioural intentions. Part Two seeks to determine if the potential exists for consumer detriment. This part introduces the construct of match/mismatch, investigating whether or not respondents' interpretation was consistent with the DTCGT results presented. This construct allows charting of the effect of interpretation on affect and behavioural intentions.

Part Three assesses the likelihood of exposure to potential consumer detriment by investigating the likelihood of purchasing from DTCGT companies operating under different business models. Results are also presented for respondents' willingness to participate in DTCGT research depending on its declared use, as well as their overall confidence in the DTCGT offering.

Part Four profiles respondents who mismatch − those who made inconsistent interpretations. Much of the empirical research discussed in Chapter Four focused on those who made consistent − or often labelled 'accurate' − interpretations. This section seeks to fill a gap in the existing research seeking to gain insight into those respondents who might mismatch.

Finally, Part Five addresses both the strengths and limitations of the survey and its analysis. Appendix Five provides results of MANOVAs conducted.

# PART ONE: CONTEXT FOR DTCGT ENGAGEMENT

Perception refers to the way individuals select, organise, and interpret stimuli in the world around them, with each individual's perceptual set representing the sum total of their personal characteristics, knowledge, attitudes and life experience.[3] Each respondent's perceptual set functions as the context through which they both interpret and implement DTCGT results. Of particular significance would be their personal characteristics such as gender and age, health status including family disease history, and pre-existing health-related knowledge, attitudes and behaviours. Whether these affected their engagement with DTCGT results or resulted in differential vulnerability to any harm identified was of interest.

## *6.1.1 Personal context: Personal characteristics and health status*

### *6.1.1.1 Personal characteristics*

Overall, under half of respondents in both countries were married, one-third had children, with most tertiary educated, in paid employment, and in the lower to moderate-income ranges. As expected, younger respondents from both Australia[4] and the US were the ones much more likely to have children and be in paid employment, however no other substantive differences were found between the two countries (Table 6.1). As such, the broad similarity between the two samples was not judged of concern relative to skewing results when countries were compared.

[3] See Jan Charbonneau, Michael Solomon, Greg Marshall and Elnora Stuart, *Marketing: Real People, Real Choices* 2e (Pearson New Zealand, 2011), Chapter Four.
[4] For ease of reading Australia is often referred to as AU.

**Table 6.1 Personal characteristics: AU and US**

| Personal characteristics | Country | |
|---|---|---|
| % | AU | US |
| *Gender* | | |
| Male | 49.0 | 49.0 |
| Female | 51.0 | 51.0 |
| *Age group* | | |
| 18 – 24 years old | 12.6 | 13.4 |
| 25 – 44 years old | 34.3 | 34.6 |
| 45 – 64 years old | 35.3 | 34.2 |
| Aged 65+ | 17.8 | 17.8 |
| *Younger/older* | | |
| Younger (18 – 44) | 46.9 | 48.0 |
| Older (45+) | 53.1 | 52.0 |
| *Marital status* | | |
| Married | 59.3 | 58.0 |
| Not married | 40.7 | 42.0 |
| *Children* | | |
| Yes | 30.1 | 36.8 |
| No | 69.9 | 63.2 |
| *Education* | | |
| Secondary school | 36.8 | 24.0 |
| College/university | 48.5 | 63.9 |
| Postgraduate | 14.7 | 12.1 |
| *Employment* | | |
| Paid | 48.9 | 52.8 |
| Not paid | 43.5 | 42.9 |
| Student | 7.6 | 4.3 |
| *Income* | | |
| Under $50,000 (lower) | 35.8 | 46.3 |
| Under $150,000 (moderate) | 45.3 | 41.0 |
| Over $150,000 (higher) | 6.1 | 9.0 |
| Prefer not to answer | 12.8 | 3.7 |

### 6.1.1.2 Health status

The majority in both countries rated their health as average or above average with over a third reporting either healthy or unhealthy lifestyles.[5] While the majority declared no family history of either disease, US respondents were much more likely to declare family histories of both. Of particular concern are those who reported being 'not sure' as to family history, especially relative to Cancer (AU 18%; US 13%) as they may not engage in mitigation strategies such as increased screening or lifestyle alterations. Overall about half were taking prescription drugs, with older respondents much more likely, as would be expected (Table 6.2).[6]

**Table 6.2 Health status: AU and US**

| **Health status** | **Country** | |
|---|---|---|
| % | AU | US |
| *Health self-report* | | |
| Below average | 18.2 | 13.3 |
| Average | 47.5 | 41.4 |
| Above average | 34.3 | 45.2 |
| *Lifestyle* | | |
| Unhealthy | 35.2 | 39.6 |
| Moderately healthy | 26.9 | 25.0 |
| Healthy | 37.9 | 35.4 |
| *Family history – Type 2 Diabetes* | | |
| Yes | 26.0 | 38.4 |
| No | 60.6 | 52.4 |
| Not sure | 12.1 | 8.6 |
| Prefer not to answer | 1.3 | 0.6 |
| *Family history – Colorectal Cancer* | | |
| Yes | 7.2 | 12.1 |
| No | 73.0 | 74.4 |
| Not sure | 18.3 | 13.0 |
| Prefer not to answer | 1.5 | 0.5 |
| *Prescription drug usage* | | |
| Yes | 48.3 | 54.9 |
| No | 49.6 | 43.0 |
| Prefer not to answer | 2.1 | 2.1 |

[5] 14% of Australians and 9% of Americans rated their health as fair or poor. Australian Institute of Health and Welfare, Australia's Health 2016: In brief (2016) Cat. no AUS201: Canberra, AIHW, pg. 3; National Center for Health Statistics, Health, United States 2016, Hyattsville, MD, 2017, Table 45, 203-204.

[6] See Chapter Five Section 5.2.1.2 for discussion of prescription drug usage in AU and US.

## 6.1.2 Health-related context

### 6.1.2.1 Health-related skills: Health numeracy

Respondents were asked two health numeracy questions – one for risk numeracy and one for pills numeracy. The majority of respondents were able to correctly answer both questions, although AU respondents were much more likely than their US counterparts to provide correct answers (Chart 6.1).[7] Those providing incorrect answers are of concern, especially for risk numeracy, as this may affect results interpretation. Health numeracy did not significantly vary inter-respondent, although older US respondents exhibited high pills numeracy.

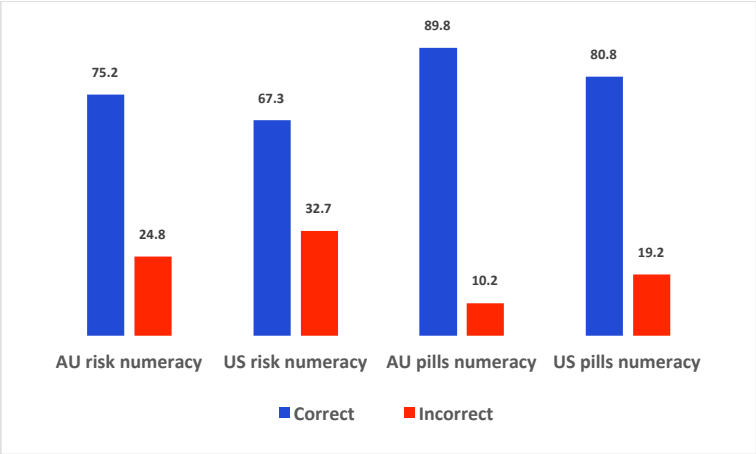


**Chart 6.1 Health numeracy (%)**

### 6.1.2.2 Health-related attitudes: Health beliefs & trust in sources of health information

#### *Health beliefs*

Confirmatory factor analysis reduced the individual health attitudes tested into two factors: health active, indicating active involvement in one's health; and health passive, indicating passive involvement (Chart 6.2).[8] For example, health active individuals were more alert to health changes and took responsibility for their health, believing their actions impacted both health and disease development, even if genetics-related. Health passive individuals only worried when sick and believed illness and disease could not be controlled. Overall, respondents expressed higher mean health active than health passive scores, with AU respondents expressing both lower mean health active and health passive scores than their US counterparts. Whether health active and health

[7] Those providing correct answers referred to as having high risk or pills numeracy, with those providing incorrect answers low risk or pills numeracy.
[8] See Appendix Four.

passive attitudes exerted an influence on the various aspects of engagement was of interest in this research, with its effect tested relative to engagement with DTCGT results.

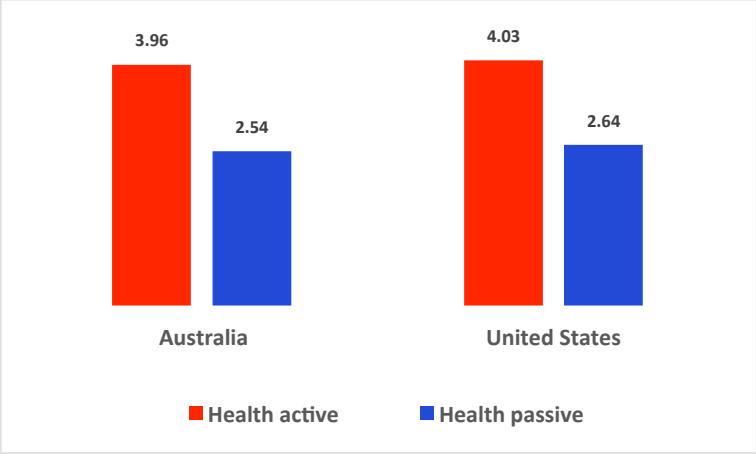


**Chart 6.2 Mean health active & health passive**

AU and US respondents who were older, with above average health, and healthy lifestyles were more health active, while those with children, who were younger, and had lower health numeracy were more health passive. Of concern are respondents with children who do not take an active approach to healthcare, although this must be approached with caution given the smaller number of respondents having children.

AU respondents who were married and exhibited higher health numeracy, and US respondents with postgraduate educations and higher incomes were more health active. AU respondents who were students, and reported average health and unhealthy lifestyles were more health passive. While US males were clearly more health passive, other US results were inconsistent; for example high-income earners and those with above average health were both more health active and more health passive.

### *Genetic literacy*

While not tested specifically, the general genetics as well as diabetes and cancer-specific attitude questions included in the suite of health attitudes provide a rough indicator as to respondent genetic literacy (Table 6.3). Overall, respondents appeared to appreciate the importance of lifestyle and family history to the development of both diabetes and cancer, as noted by the higher means for positively phrased statements and lower means for those negatively phrased. Of interest is the similarity between AU and US attitudes, with the exception of not being able to control genetics, where US respondents expressed higher mean agreement. While testing for genetic literacy was not incorporated into subsequent analysis, respondent genetic literacy was not judged to be of concern.

**Table 6.3 Genetic literacy: AU and US**

| Disease-related attitudes | Country | |
|---|---|---|
| Means* | AU | US |
| *Disease – general attitude* | | |
| Cannot prevent illness | 1.50 | 1.60 |
| *Genetics – specific attitudes* | | |
| Can control – genetics | 2.19 | 2.25 |
| Cannot control – genetics | 1.60 | 1.76 |
| *Diabetes & Cancer-specific attitudes* | | |
| Lifestyle is important – Diabetes | 2.74 | 2.73 |
| Family history not important – Diabetes | 1.48 | 1.56 |
| Can prevent – Diabetes | 2.77 | 2.70 |
| Lifestyle is not important – Cancer | 1.57 | 1.68 |
| Family history is important – Cancer | 2.56 | 2.62 |
| Cannot prevent – Cancer | 1.79 | 1.87 |

* Recodes used.

### *Trust in sources of health information*

Trust plays a role in terms of both where information is sought and whether information, including recommendations, is believed and possibly actioned. Respondents in both countries expressed the their highest mean trust in doctors, consistent with published research.[9] AU respondents expressed lower mean trust in the Internet and health communities than their US counterparts (Chart 6.3).

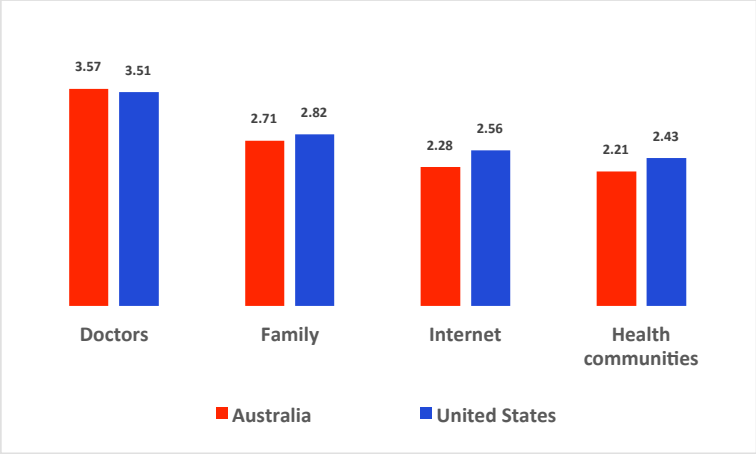


**Chart 6.3 Mean trust in sources of health information**

AU respondents with high trust in doctors and US respondents with high trust in the four sources exhibited the highest mean health active scores. AU respondents with low trust in doctors and

[9] Robert Blendon, John Benson and Joachim Hero, 'Public Trust in Physicians – U.S. Medicine in International Perspective' (2014) 371(17) *New England Journal of Medicine* 1570-1572.

high trust in family, the Internet and health communities exhibited higher mean health passive scores, with US respondents exhibiting similar patterns.

### 6.1.2.3 *Health-related behaviours*

While past health-related behaviours do not predict future behaviours, they do provide an indication as to respondents' typical health-related behaviours and allow comparison with their stated behavioural intentions post-DTCGT testing. Mean frequency of engaging in the tested behaviours was comparatively low in both countries. However, AU respondents consistently reported lower frequency of online searching, self-diagnosis, and sharing of health and genetic information than their US counterparts, consistent with their lower trust in online sources of health information (Chart 6.4). The most frequently engaged in behaviour was discussing health issues with family, however this only occurred occasionally, perhaps helping to explain why some respondents were uncertain as to family history.

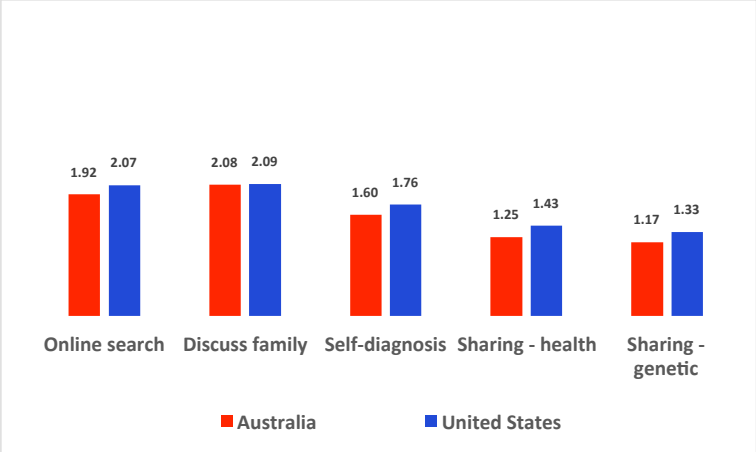


**Chart 6.4 Mean frequency of health-related behaviours**

AU respondents who reported regular searching and discussing with family but never sharing health or genetic information exhibited higher mean health active scores. US respondents who regularly searched, discussed with family and regularly shared genetic information expressed higher mean health active scores. AU respondents who regularly self-diagnosed and shared both health and genetic information exhibited higher mean health passive scores, with similar patterns found for US respondents. Younger US respondents and those with children were much more likely to self-diagnose and share both health and genetic information online. This is somewhat concerning – while there are reputable and accurate online health information sources and diagnostic tools, there are also questionable ones.

### 6.1.3 Familiarity and prior purchase

Familiarity with DTCGT and prior purchase were low for AU respondents, with less than 10% being familiar (US 24%) and 10% having previously purchased (US 21%), consistent with published Australian research, as discussed in Chapter Two (2.3.3).[10] Taken together, familiarity and prior purchase confirm both AU and US samples contained a relatively low proportion of early adopters, as was hoped.

### 6.1.4 Personal context for AU respondents: An overview

Overall, AU respondents expressed low familiarity and prior purchase, tended to be single, without children and tertiary educated in lower to moderate-income employment. They reported their health as average to above average and no family history of diabetes or cancer, with most taking prescription drugs, similar to their US counterparts. AU respondents generally had higher health numeracy than their US counterparts, were actively involved in their health, and exhibited reasonable genetic literacy. Like their US counterparts, they expressed high trust in doctors, however trust in family, the Internet and health communities was lower. Overall, frequency of health-related behaviours was low, although discussing with family was the highest.

When relationships were explored, the following overall patterns emerged for both AU and US respondents. As trust in both the Internet and health communities *increased*, the frequency of using the Internet to search for health-related information, self-diagnosis and sharing of health and genetic information *increased*.[11] As familiarity *increased*, so too did frequency of online sharing of both health and genetic information. Interestingly, for AU respondents as trust in doctors *increased*, the frequency of using the Internet for self-diagnose and information sharing *decreased*. AU trust in doctors was significantly higher than trust in the Internet or health communities and familiarity was quite low, perhaps helping to explain lower AU frequency of engaging in online-related health behaviours.

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[10] Sylvia Metcalfe, Chriselle Hickerton, Jacqueline Savard, Bronwyn Terril, Erin Turbitt, Clara Gaff, Kathlene Gray, Anna Middleton, Brenda Wilson and Ainsley Newson, 'Australian's views on personal genomic testing: focus group findings from the Genioz study' (2018) *European Journal of Human Genetics* <https://doi.org/10.1038/s41431-018-0151-1; Jacqueline Savard, J Mooney-Somers, Ainsley Newsom and Ian Kerridge, 'Australian's knowledge and perceptions of direct-to-consumer personal genome testing' (2014) 44(1) *Internal Medicine Journal* 27-31; Christine Critchley, Dianne Nicol, Margaret Otlowski and Don Chalmers, 'Public reaction to direct-to-consumer online genetic tests: Comparing attitudes, trust and intentions across commercial and conventional providers' (2014) *Public Understanding of Science* DOI: 10.1177/0963662513519937.

[11] The Internet and health communities were strongly related for both countries.

# PART TWO: ENGAGING WITH DTCGT RESULTS: IS THERE THE POTENTIAL FOR CONSUMER DETRIMENT?

Part Two represents the core of this research as it explores respondent engagement with DTCGT tests and reports the results of experimentation component. As DTCGT companies' business model is based on bundled tests, of key interest is whether respondent engagement differed for the three sets of DTCGT sample results.

## *6.2.1 We got our results – What did they mean?*

*'Problems of user comprehension are hugely magnified in this kind of health report. Customers are being asked to understand what a marginal change in disease risk means for their overall health; the type of evidence, from population-wide studies, that supports the effects of these low-impact mutations; how the test provider is compounding the effects of many variants together; and the difference between absolute and relative risk — the kind of statistical thinking that says a 20% change to a 10% risk adds up to 12 and not 30.'*[12]

*'More than 90% of our customers have the comprehension, which means the average individual in this country can understand genetic information.'*[13]

As discussed in Chapters Three and Four, one of, if not *the* most, significant concerns raised relative to DTCGT is the necessity of self-interpretation of complex DTCGT results – as evidenced by the first quote. The industry however does not appear to share this concern – as evidenced by the second quote.

So, which quote is closer to the reality of DTCGT interpretation? Two separate aspects were investigated relative to respondent comprehension of their randomly allocated DTCGT results: self-report understanding for diabetes, cancer and drug sensitivity tests, and contextual interpretation for the two disease predisposition tests.[14]

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[12] Aaron Krol, 'What comes next for Direct-to-Consumer Genetics?', www.bio-itworld.com, 16 July 2015.
[13] Anne Wojcicki, CEO of US Direct-to-consumer genetic testing company 23andMe: presentation at the Future of Genomic Medicine IX conference, San Diego, California, March 2016, as reported in Damian McNamara, '23andMe opens up about Direct-to-Consumer Genetic Testing', www.medscape.com, 10 March 2016.
[14] Respondents were randomly allocated into one of three risk treatments for diabetes and cancer based on the average person's risk – *Low* minus 20%, *High* plus 20% and *Higher* plus 100%. Respondents were randomly allocated into either *Slow* or *Fast* metaboliser for drug sensitivity but were not asked specifically to interpret results.

### 6.2.1.1 *Understanding of sample DTCGT results*

Self-report understanding provides insight into the context within which respondents interpret test results and an admittedly broad indication as to respondent comfort in their interpretation.

*Does understanding differ by DTCGT test?*

One-way repeated measures ANOVAs were conducted to compare understanding scores for the three DTCGT tests (Chart 6.5). Results by both test and country indicated reasonably high mean understanding. However this did vary in all instances across the three tests suggesting independent evaluation. AU respondents expressed lower mean understanding than their US counterparts for the three tests, with all respondents expressing the lowest mean understanding for the drug sensitivity test. Even though presented last ensuring respondents had some experience with results, lower understanding for the drug sensitivity test may suggest issues with the metabolisation rate terminology used. While over three-quarters of respondents found the diabetes and cancer results easy to understand, this dropped to under half for the drug sensitivity results, with more expressing neutral opinions, especially so for AU respondents. This variation in levels of understanding represents a concern generally given the DTCGT practice of bundling tests.

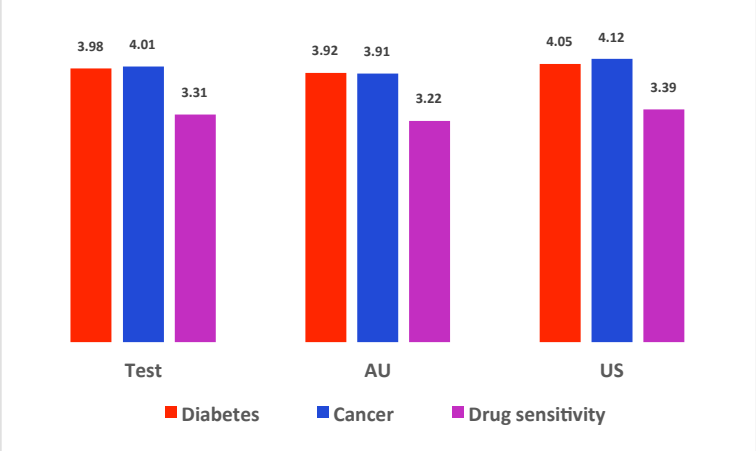


**Chart 6.5 Mean Understanding: By test & country**

AU and US respondents who found test results easy to understand exhibited higher mean health active scores for all three tests. AU respondents who were neutral exhibited higher mean health passive scores for all three tests. US respondents who found diabetes test results harder to understand and drug sensitivity results easier to understand exhibited higher mean health passive scores.

While these results would appear to confirm the industry quote at the beginning of this section, they must be approached with caution. From a respondent perspective, *understanding* may

simply be assigning objective meaning to the words used e.g. diabetes = disease. This may not, however, translate into *interpretation*, the more subjective process of explaining or advancing an opinion as to what something means in a particular context.

#### 6.2.1.2 *Disease-predisposition tests: What did results mean to us?*

Interpretation of the disease predisposition results had both objective and subjective components: the actual DTCGT results received and how each respondent interpreted them (Table 6.4). The objective component was the three risk treatments used for both diabetes and cancer, referred to as *Actual severity* (AS) with individual treatments labelled as AS(Low), AS(High) and AS(Higher) to reflect -20%, +20% or +100% of the average person's risk. Respondents were randomly allocated into one treatment each for both diabetes and cancer, with quotas imposed to ensure equal distribution. The subjective component was respondent interpretation of their allocated treatment for both diseases, referred to as *Perceived severity* (PS) with individual response categories labelled as PS(Lower), PS(Higher), PS(Same) and PS(Not sure). Even though a comparatively small number selected PS(Not sure), it was retained as it represented a distinct and informed response. For example, a respondent allocated AS(Low), representing the average person's risk -20%, who believed their personal risk was higher than the average person's selected 'higher', denoted as PS(Higher). An individual allocated AS(Higher), representing the average person's risk +100%, who believed their personal risk was about the same as the average person's selected 'same', denoted as PS(Same).

**Table 6.4 Random allocations & response options: Disease predisposition tests**

| Response options: | Random allocation: *Actual severity* | | |
|---|---|---|---|
| *Perceived severity* | AS(Low) | AS(High) | AS(Higher) |
| PS(Lower) | PS(Lower) | PS(Lower) | PS(Lower) |
| PS(Higher) | PS(Higher) | PS(Higher) | PS(Higher) |
| PS(Same) | PS(Same) | PS(Same) | PS(Same) |
| PS(Not sure) | PS(Not sure) | PS(Not sure) | PS(Not sure) |

*Did interpretation differ by disease?*

Statistically significant differences were found for both diabetes and cancer between allocated risk (AS) and subjective interpretation (PS). For both diseases, the effect of AS on PS was moderate verging on large, suggesting the specific test results presented had an influence on how results were interpreted.

The same overall pattern of responses was observed for both tests, although the actual percentages in each interpretation category differed (Charts 6.6 & 6.7). Respondents allocated AS(Low) were much more likely to interpret PS(Lower) and much less likely to interpret PS(Higher). Those allocated AS(High) or AS(Higher) were much more likely to interpret PS(Higher) and much less likely to interpret PS(Lower).[15]

Comparing percentages illustrates respondents differentiated between AS(High) and AS(Higher) when interpreting PS(Higher). For both tests, respondents allocated AS(High) were much more likely to interpret PS(Same) but those allocated AS(Higher) were much less likely, especially so for cancer. For both tests across all AS categories, a comparatively small number of respondents selected PS(Not sure), suggesting respondents selecting the other interpretation categories were reasonably confident in their interpretations.

For cancer, more respondents interpreted PS(Same), especially for those allocated AS(Low) and AS(High). While risk numeracy was found to exert a moderate effect on interpretation in several instances, its effect was not consistent across risk treatments, diseases or countries so respondent facility with numbers did not fully explain differences. Perhaps, the numeric differentials for these AS levels (+/- 20%) compared to the average person's lifetime risk of 4.0% (*cf.* Diabetes 20.7%) may not have been as obvious or easy to calculate, or respondents judged the average risk of cancer as significantly lower overall than diabetes and therefore not as much of a concern.

[15] With the exception of those allocated AS(High) for Cancer where the adjusted residual for PS(Higher) was 3.0, marginally below the 3.3 cut-off.

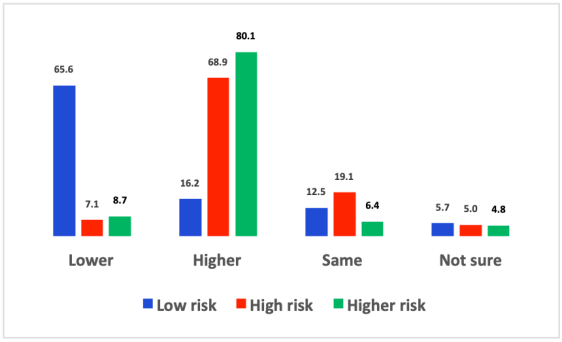


**Chart 6.6 Interpretation (%): Diabetes**

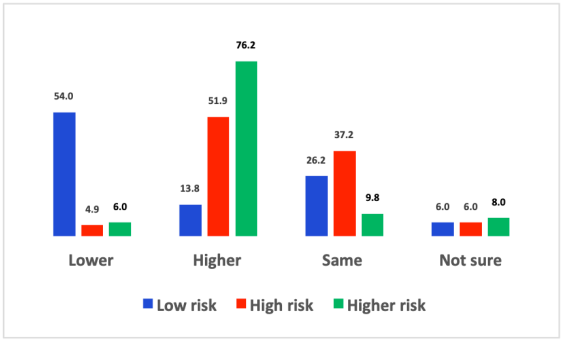


**Chart 6.7 Interpretation (%): Cancer**

Of note were the number of respondents judging AS(Low) and AS(High) as 'about the same', especially for cancer. As noted in Chapter Four (4.1.1.5), most consumers would have predicted risks 'close' to average, yet it would appear a reasonable number consider +/-20% as 'close', especially so for +20%.

### *Did interpretation differ by country?*

The countries were first looked at separately to establish patterns within each country's data and then compared. For Australia, the effect of actual severity (AS) on perceived severity (PS) was large for both diseases, suggesting again the specific test results presented had an influence on how results were interpreted (Chart 6.8). AU respondents allocated AS(Low) for both diabetes and cancer were much more likely to interpret PS(Lower) and much less likely to interpret PS(Higher). Those allocated AS(High) or AS(Higher) were much more likely to interpret PS(Higher)[16] and much less likely to interpret PS(Lower). For both diabetes and cancer, respondents allocated AS(High) were much more likely to interpret PS(Same) but those allocated AS(Higher) were much less likely, especially so for cancer.

[16] With the exception of those allocated AS(High) for Cancer.

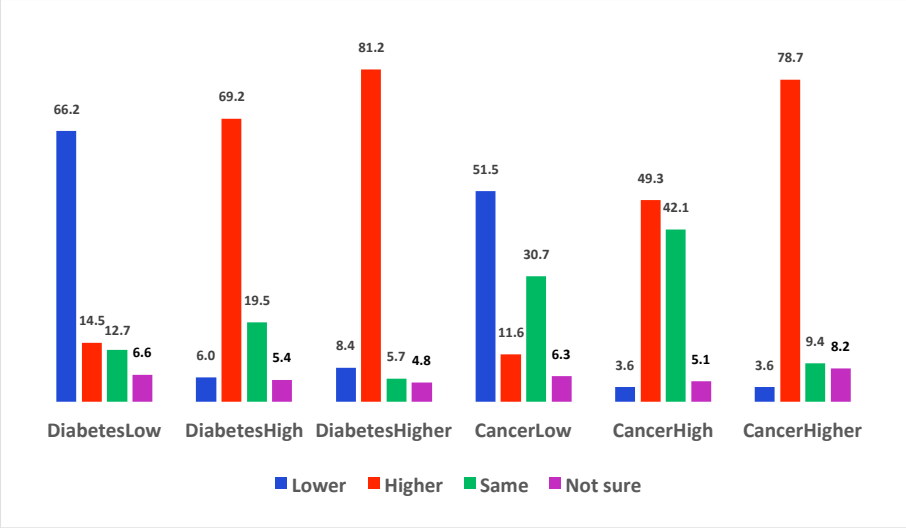


**Chart 6.8 Interpretation (%): Diabetes & Cancer (AU)**

The same overall pattern of responses identified in the AU data was also observed in US data for both tests (Chart 6.9). US respondents allocated AS(Low) for both diabetes and cancer were much more likely to interpret PS(Lower) and much less likely to interpret PS(Higher). Those allocated AS(High) or AS(Higher) were much more likely to interpret PS(Higher)[17] and much less likely to interpret PS(Lower). For both diabetes and cancer, respondents allocated AS(High) were much more likely to interpret PS(Same), but those allocated AS(Higher) were much less likely, especially so for cancer.

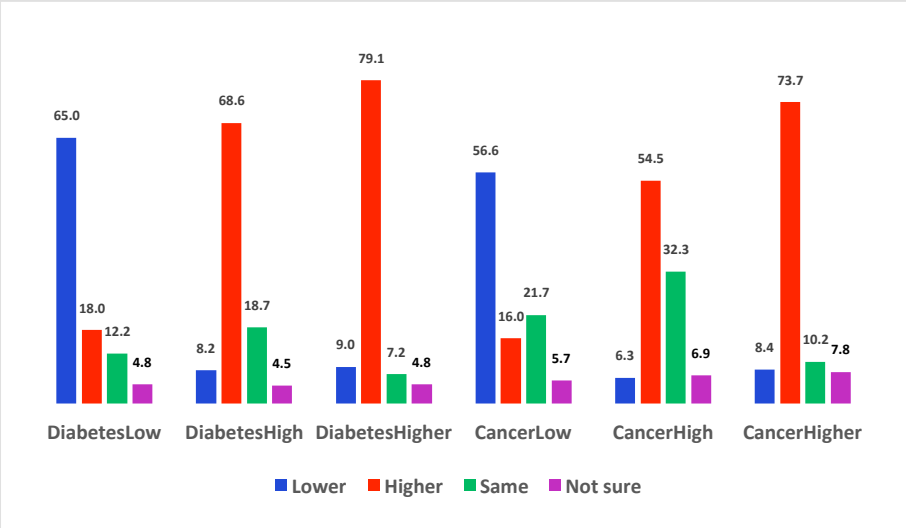


**Chart 6.9 Interpretation (%): Diabetes & Cancer (US)**

When compared by test, the data highlights, in particular, the larger number of AU respondents interpreting AS(Same) for cancer, explaining the comparatively lower PS(Lower) and PS(Higher) percentages. However, when the two countries were compared, no statistically significant

[17] With the exception of AS(High) for cancer where the adjusted residual was just below the 3.3 cut-off.

differences were found for either diabetes or cancer. No substantial or consistent inter-respondent differences were found across the three risk allocations for diabetes and cancer in AU and US. As such, personal characteristics and health status were not found to exert any influence for diabetes or cancer in either country.

### *Contextualising interpretation: Match/mismatch*

To analyse broad patterns in the data, new variables were created for each disease: Match/mismatchD for diabetes and Match/mismatchC for cancer. The term 'match' is used to denote congruence or consistency (PS = AS), with 'mismatch' used to denote incongruence or inconsistency (PS < AS; PS > AS; PS ≈ AS) from an objective, numeric perspective.[18] Terms such as 'accurate' or 'correct' were avoided as they implicitly include value judgements based on subjective criteria.

For each disease, respondent scores for those matching in their allocated AS group were combined e.g. AS(Low) interpreting as PS(Lower). Scores for those who mismatched were also combined e.g. AS(Low) interpreting as PS(Higher) + AS(Low)/PS(Same). PS(Not sure) responses were eliminated to allow focus on interpretations where respondents had reasonable comfort.[19] The 'match/mismatch' construct, as illustrated in Table 6.4, adjusts for the random allocation, allowing focus on whether *how* individuals interpreted results was consistent or inconsistent, regardless of actual results allocated, rather than *what* was their specific interpretation.

**Table 6.5 Match/mismatchD and Match/mismatchC: How variables created for each**

| Response options: | Random allocation: *Actual severity* | | |
|---|---|---|---|
| *Perceived severity* | AS(Low) | AS(High) | AS(Higher) |
| PS(Lower) | **PS(Lower)** | *PS(Lower)* | *PS(Lower)* |
| PS(Higher) | *PS(Higher)* | **PS(Higher)** | **PS(Higher)** |
| PS(Same) | *PS(Same)* | *PS(Same)* | *PS(Same)* |
| PS(Not sure) | ~~PS(Not sure)~~ | ~~PS(Not sure)~~ | ~~PS(Not sure)~~ |

* Responses combined into Match for each disease are denoted in **bold**; responses combined into Mismatch for each disease are denoted in *italics*; responses not included for each disease are denoted as ~~strikethrough~~.

Overall, 75% of respondents matched for diabetes and 65% for cancer (Chart 6.10). When compared by disease, although the effect was small, those matching for one disease were much more likely to match for the other, while those mismatching for one mismatched for the other,

[18] As used in geometry to describe objects of the same size and shape or mirror image

[19] Eliminating PS(Not sure) (103 D & 133 C) resulted in 1897 responses for diabetes (AU 944; US 53) and 1867 for cancer (AU 935; US 932). Valid percentages (out of 100%) are used and should be read as 'Of the people who matched/mismatched for diabetes, 75.4% matched and 24.6% mismatched.'

again a concern relative to DTCGT's bundled nature. While these results are consistent with much of the empirical research discussed in Chapter Four – *most do, some don't* – looking at actual numbers suggest cause for concern as 466 individuals (out of 2000) mismatched for diabetes and 654 for cancer, not insubstantial numbers.

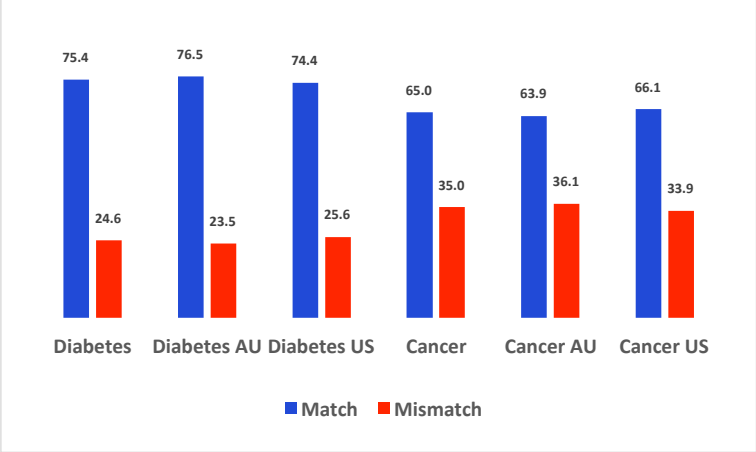


**Chart 6.10 Match/mismatch (%): By disease & country**

No inter-country differences were found for either disease, but were by respondent. For diabetes, respondents in both countries who matched expressed higher understanding of the diabetes results and trust in doctors, while those who mismatched expressed higher health passive scores and frequency of online sharing of both health and genetic information. AU respondents who matched expressing higher health active scores and US respondents who mismatched higher trust in health communities and frequency of self-diagnosis.

For cancer, respondents in both countries who matched expressed higher health active scores, while those who mismatched expressed higher health passive scores. AU respondents who matched expressed higher understanding of the cancer results. US respondents who matched expressed higher trust in doctors while those who mismatched exhibited higher frequency of sharing genetic information. This seems to suggest respondents' overall attitude towards their health (health active and health passive) may have influenced how they interpreted DTCGT results.

*Across diseases: Match/mismatchDC*

To adjust for differences by type of test, a new variable was created with three categories: respondents who matched for both diabetes and cancer (MatchDC); those who mismatched for both diseases (MismatchDC); and respondents who matched/mismatched for one disease or selected PS(not sure) for one disease (Inconsistent). Respondents who selected PS(Not sure) for both diseases were eliminated. When viewed across diseases, 52% of respondents matched, 11% mismatched and 37% were inconsistent, with no differences found by country (Chart 6.11). When viewed this way, the picture that emerges raises more cause for concern, especially given DTCGT's bundled nature. While 956 individuals matched for both diabetes and cancer, 198 consistently mismatched, while 680 were inconsistent.

No differences were found inter-country but were for respondents. Overall, AU respondents who matched exhibited higher health active scores while those who mismatched exhibited higher health passive scores, familiarity and sharing of health and genetic information. US respondents who were inconsistent expressed higher health active scores and those who matched higher trust in doctors. US respondents who mismatched exhibited higher health passive scores and sharing of health and genetic information.

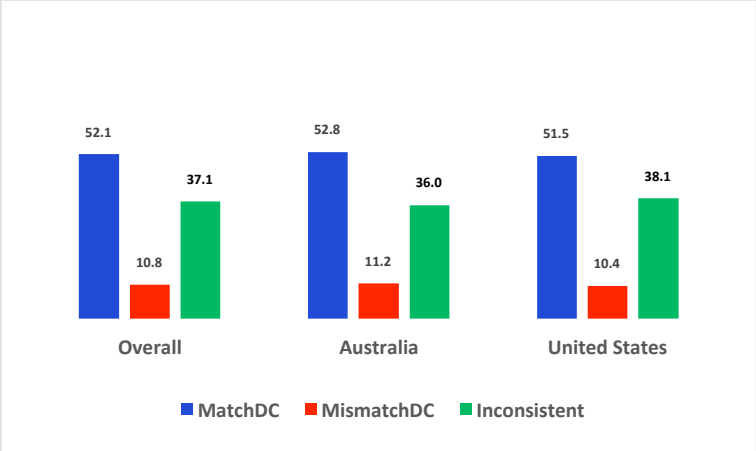


**Chart 6.11 Match/mismatchDC (%)**

When the two aspects of comprehension − self-report understanding and interpretation − are reviewed, what is noted is the similarity of patterns that emerged. While the level/intensity may differ between countries, the patterns remained consistent. While most respondents matched, the number who 'mismatched' for each disease or, when viewed across diseases, either mismatched or were inconsistent in their interpretation are of concern. As noted, *most do, some don't*. However, the *some* actually represent a not insubstantial number of individuals, suggesting the 90% comprehension of the industry quote at the beginning of this section was certainly optimistic. While inter-respondent differences were found, none would realistically provide any

consistent assistance in determining beforehand which respondents might mismatch or provide inconsistent interpretations.

The next section investigates whether interpretation inconsistencies influence the psychological outcomes experienced.

### 6.2.2 *We got our results – How did we feel?*

Confirmatory factor analysis identified two factors explaining the variation in responses for diabetes, cancer and drug sensitivity tests in both countries: *emotional distress* (comprising *anxious*, *upset*, *guilty*, *relieved*, *scared*, *nervous* and *stressed*) and *engagement* (comprising *concerned*, *interested*, *worried*).[20]

For diabetes, the largest single contributor to overall *emotional distress* was *nervous* followed by *upset* and *scared*, with *worry* followed by *concern* for overall *engagement.* For cancer, *worry* followed by *concern* contributed the most to overall *engagement*, however for overall *emotional distress* this varied with *anxiety* followed by *nervous* and *stressed* for AU and *nervous* followed by *stressed* and *scared* for US. For drug sensitivity, *concern* contributed the most to overall *engagement*. However this varied for *emotional distress* with *scared* and *stressed* contributing equally for AU and *nervous* followed by *scared* for US.

For the three tests, respondents experienced higher mean *engagement* than *emotional distress*, with mean *emotional distress* highest for cancer and mean *engagement* highest for drug sensitivity (Chart 6.12).

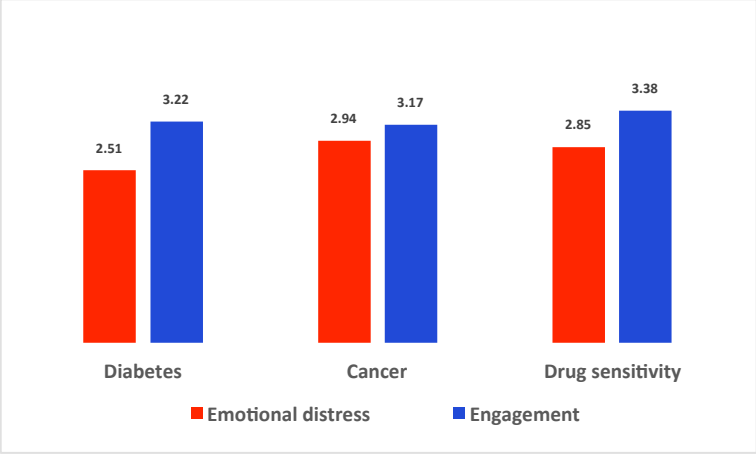


**Chart 6.12 Mean psychological outcomes: By test**

[20] 'Relieved' was reverse-scored for confirmatory factor and MANOVA analysis. Relieved and worried were removed from factor loading for Drug sensitivity.

### 6.2.2.1 Did psychological outcomes differ by test, country or respondent?

Repeated measures ANOVA results found statistically significant differences between the mean scores for each of the three tests in each of the countries (Chart 6.13). In all instances, mean *engagement* was higher than mean *emotional distress*.

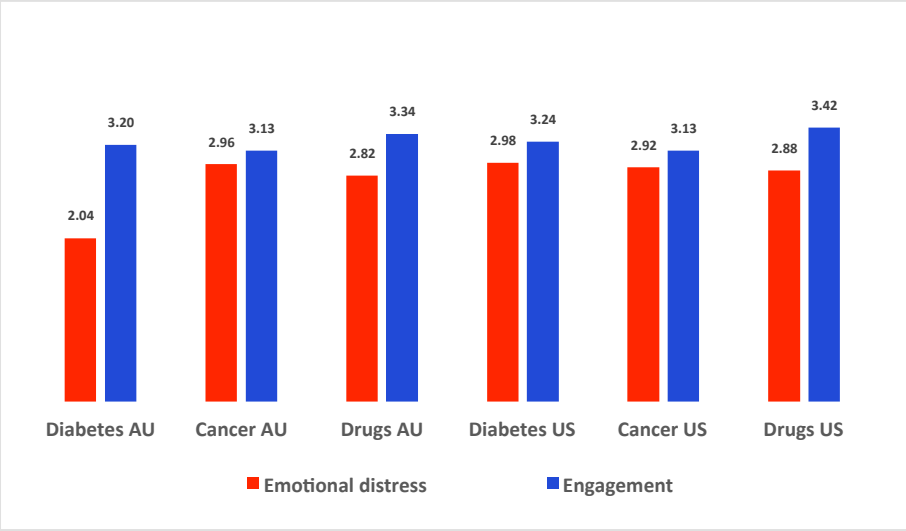


**Chart 6.13 Mean psychological outcomes: By country**

Respondents in both countries experienced higher mean *engagement* than *emotional distress*. AU respondents experienced the highest *emotional distress* for cancer and the highest *engagement* for drug sensitivity, while US respondents experienced significantly higher *emotional distress* for diabetes and also the highest *engagement* for drug sensitivity. For diabetes, AU and US respondents experienced higher *emotional distress* if they had children, low risk numeracy, frequently shared health and genetic information online, higher familiarity and had purchase experience and higher *engagement* if they had higher trust in family.

For cancer, AU and US respondents with low risk numeracy, who frequently shared genetic information only and again had purchased experienced higher *emotional distress*. AU and US respondents with higher trust in families experienced higher *engagement* for diabetes, with low risk numeracy generating higher *engagement* for Cancer. For drug sensitivity, AU and US respondents with low pills numeracy, those who regularly shared health and genetic information, and had purchase experience, experienced higher *emotional distress* while females and those who regularly discussed with family experienced *higher engagement*.

### 6.2.2.2 Disease predisposition results: Did interpretation matter?

To determine whether the two aspects of interpretation tested – actual severity (allocated personal risk) and perceived severity (interpretation of personal risk) – influenced the level of

*emotional distress* and *engagement* experienced relative to diabetes and cancer, individual 3 (AS(Low), AS(High), AS(Higher)) by 4 (PS(Lower), PS (Higher), PS(Same), PS(NotSure)) Multivariate Analysis of Variance (MANOVA) were conducted. As the confirmatory factor analysis indicated *emotional distress* and *engagement* were highly correlated, a MANOVA was appropriate to assess mean differences across the 12 groups (3 x 4) for each disease. To investigate whether there were any unique effects for *emotional distress* and *engagement*, separate 3 x 4 ANOVAs for each disease were also conducted. To determine whether the influence of actual severity or perceived severity on *emotional distress* and *engagement* varied across country for each disease, a 3 (AS) x 4 (PS) x 2 (AU, US) MANOVA and individual ANOVAs were conducted.[21]

### *Diabetes*

MANOVA analysis suggested actual severity and perceived severity individually had a significant effect on the combination of *emotional distress* and *engagement*. AS and PS individually also had a significant effect on *emotional distress* and *engagement* individually.

Actual severity was found to have an impact regardless of perceived severity, with both mean *emotional distress* and *engagement* lowest for those allocated AS(Low) and highest for those allocated AS(Higher). The same pattern was found for both countries with mean *emotional distress* and *engagement* each clearly increasing as AS allocation changed (low →high →higher), with the effect more pronounced for *engagement*. US respondents however experienced higher mean *emotional distress* and *engagement* at all AS levels, especially so for *emotional distress*.

Perceived severity was also found to have an impact regardless of actual severity, with both mean *emotional distress* and *engagement* were lowest for those interpreting their risk as PS(Lower) and highest for those interpreting PS(Higher). Again, mean *engagement* was higher than mean *emotional distress* in all instances for both countries. US respondents however experienced higher mean *emotional distress* and *engagement* at all PS levels.

Comparison of effect sizes suggest the effect of PS on *emotional distress* was almost 13 times as strong as that of AS, and over 14 times as strong for *engagement*. As such, while both aspects of interpretation have an effect, clearly the effect of individuals' interpretation of the personal risk presented in DTCGT results is stronger.

[21] See Appendix Five: MANOVA analysis.

An interaction effect was also found between AS and PS, with the two components of interpretation working together to increase both *emotional distress* and *engagement*. Again, in all instances, mean *engagement* was higher than mean *emotional distress* (Charts 6.14 – 6.17).

For example, consider respondents allocated into AS(Low) in Charts 6.14 and 6.16. In both countries, respondents who interpreted their risk as PS(Higher) experienced higher mean *emotional distress* and *engagement* compared to their counterparts who interpreted as PS(Lower). They also experienced higher mean *emotional distress* and *engagement* than those allocated AS(High) who interpreted PS(Higher), especially pronounced for US respondents. Interestingly, respondents allocated AS(Low) who interpreted their results as PS(Same) or PS(Not sure) experienced higher mean *emotional distress* and *engagement* than those interpreting PS(Lower).

Those allocated AS(High) who interpreted their results as PS(Same) or PS(Not sure) experienced lower mean *emotional distress* and *engagement* than those interpreting PS(Higher). Those allocated AS(Higher) who interpreted their risk as PS(Same) or PS(Not sure) also experienced lower mean *emotional distress* and *engagement* than those interpreting PS (Higher).

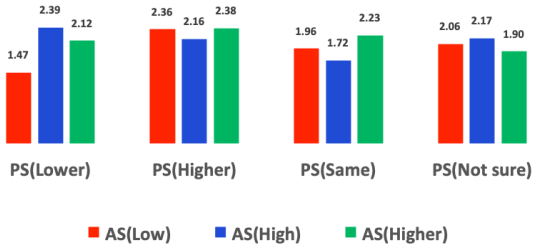


**Chart 6.14 Mean Emotional distress (Diabetes): AU**

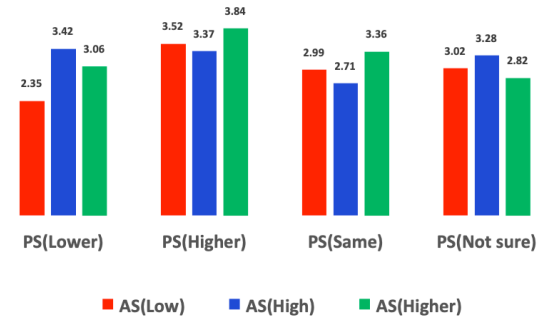


**Chart 6.15 Mean Engagement (Diabetes): AU**

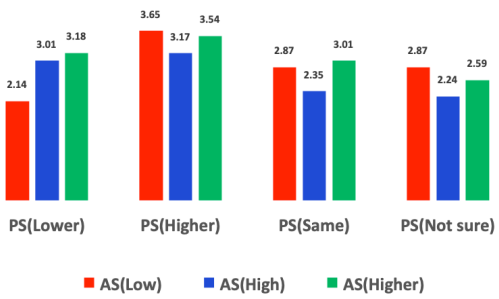


**Chart 6.16 Mean Emotional distress (Diabetes): US**

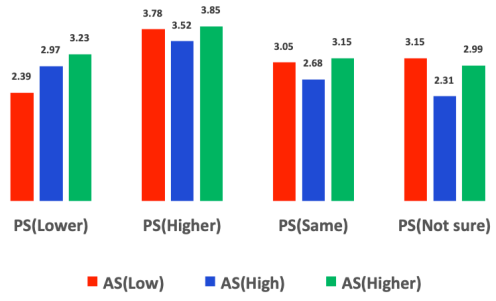


**Chart 6.17 Mean Engagement (Diabetes): US**

### *Cancer*

MANOVA analysis again suggested AS and PS individually had a significant effect on the combination of *emotional distress* and *engagement* and on each individually for cancer. Actual severity was found to have an impact regardless of PS, with both mean *emotional distress* and *engagement* lowest for those allocated AS(Low) and highest for those allocated AS(Higher). The same pattern was found for both countries with mean *emotional distress* and *engagement* again each clearly increasing as actual severity allocation changed (low →high →higher), with the effect also more pronounced for *engagement*. No consistent pattern as to which country's respondents experienced higher mean *emotional distress* or *engagement* was identified for cancer.

Perceived severity was also found to have an impact regardless of AS, with both mean *emotional distress* and *engagement* lowest for those interpreting their risk as PS(Lower) and highest for those interpreting PS(Higher). Again, mean *engagement* was higher than mean *emotional distress* in all instances for both countries. AU respondents in this instance generally experienced higher mean *emotional distress* and *engagement* at all perceived severity levels.

Comparison of effect sizes suggest the effect of PS on *emotional distress* was more than five times as strong as that of AS, and more than eight times for *engagement*. For all AS groups and all PS levels, mean *emotional distress* was higher for cancer than for diabetes. Additionally, PS effect sizes for cancer were higher than those for diabetes suggesting individual interpretation plays a more significant role for cancer (Cancer ED 0.071; Diabetes ED 0.051; Cancer E 0.090; Diabetes E 0.071).

An interaction effect was again found between AS and PS, with the two components of interpretation working together to increase both *emotional distress* and *engagement*. Again, in all instances, mean *engagement* was higher than mean *emotional distress* (Charts 6.18 – 6.21). Both AU and US respondents allocated into AS(Low) who interpreted as PS(Higher) experienced higher mean *emotional distress* and *engagement* than others in their allocation. AU respondents in this allocation who interpreted as PS(Higher) experienced the highest mean *emotional distress* of all respondents. They also experienced higher mean *engagement* than those allocated AS(High) who interpreted PS(Higher).

Both AU and US respondents allocated AS(Low) who interpreted PS(Same) or PS(Not sure) experienced higher mean *emotional distress* and *engagement* compared with those who interpreted PS(Lower). Respondents allocated AS(High) and AS(Higher) however who interpreted their results as PS(Same) actually experienced lower mean *emotional distress* and *engagement* than those who interpreted their risk as PS(Lower).

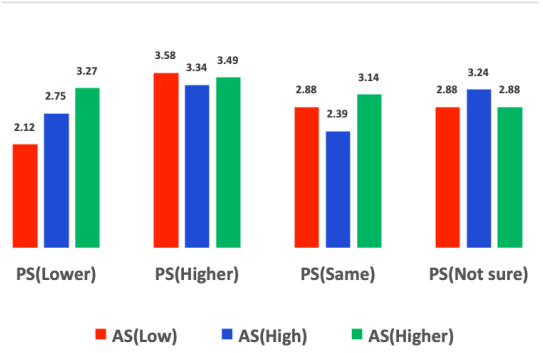


**Chart 6.18 Mean Emotional distress (Cancer): AU**

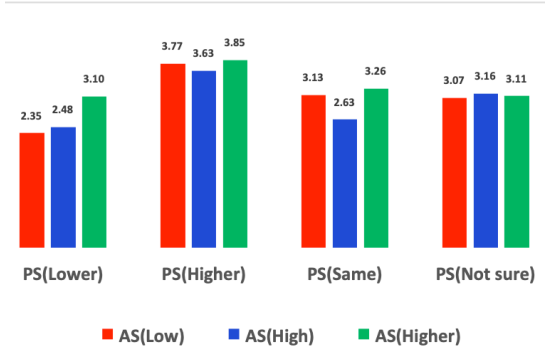


**Chart 6.19 Mean Engagement (Cancer): AU**

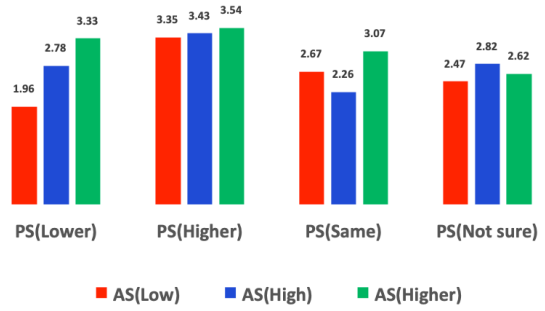


**Chart 6.20 Mean Emotional distress (Cancer): US**

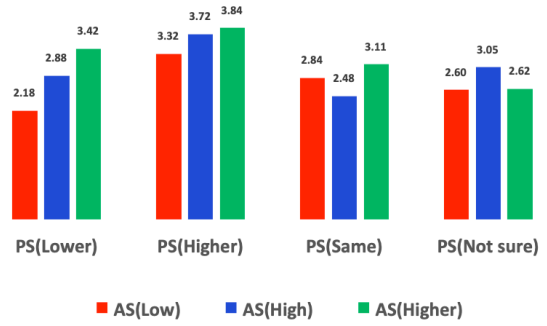


**Chart 6.21 Mean Engagement (Cancer): US**

*Implications of findings for DTCGT disease predisposition tests: Match/mismatch*

These findings suggest the actual personal lifetime risk presented in the DTCGT results (*actual severity*) and how respondents interpret the personal risk presented (*perceived severity*) independently influence respondent psychological responses. However, while both affect the *emotional distress* and *engagement* experienced by respondents, *perceived severity* was shown to exert a greater influence. Comparison of results for the two diseases suggested respondent interpretation and psychological responses might also be disease-specific (Charts 6.22 to 6.27).

If there was a match between actual severity and perceived severity (PS = AS), the *emotional distress* and *engagement* experienced function as de facto 'benchmarks', representing justified affect (psychological outcomes) based on DTCGT results.[22] Given the comparatively large number of respondents who matched, it is reasonable to consider their average responses as being 'justified' based on results. For example, respondents allocated into AS(Low) who interpreted

[22] A standard or point of reference against which things may be compared <https://en.oxforddictionaries.com/definition/benchmark>.

their risk as lower experienced lower mean *emotional distress* and *engagement* than respondents allocated into AS(High) or AS(Higher), who interpreted their risk as higher and visa-versa.

However, if there was a mismatch between actual severity and perceived severity (PS < AS or PS > AS), respondents experienced unjustified *emotional distress* and *engagement*, disproportionate to the actual personal risk identified. This is clearly in evidence when match results are compared to mismatch results. For both diseases and countries and the three AS treatments, mismatching respondents exhibited either higher or lower mean *emotional distress* and *engagement* than was warranted by the DTCGT results presented.

Mismatching occurred more often for respondents allocated AS(Low), suggesting DTCGT test results presenting a lower than average risk may be more susceptible to mismatching, and therefore potentially generate higher levels of *emotional distress* and *engagement* than are justified by the results.

Results suggest there is also potential for unjustified *emotional distress* and *engagement* for respondents who interpreted their risk was 'about the same' as the average person's risk (PS ≈ AS). For example, respondents allocated AS(Low) for both diabetes and cancer who interpreted PS(Same) experienced higher levels of *emotional distress* and *engagement* than those in AS(Low) interpreting PS(Lower). The exception was respondents allocated AS(Higher) for diabetes, who experienced higher *engagement* and equal *emotional distress*.

The following charts allow comparison across both diseases and AS levels, with those matching in each instance representing justified psychological outcomes and those mismatching disproportionate levels of *emotional distress* and *engagement*. For example, comparing Charts 6.22 through 6.27 for both diabetes and cancer clearly shows those who mismatch-higher or mismatch-same for AS(Low) experienced higher mean *emotional distress* and *engagement* than those who matched. Comparing Charts 6.26 and 6.27, those allocated AS(Higher) who mismatched for both diseases experienced disproportionately lower *emotional distress* and *engagement* than warranted by DTCGT results.

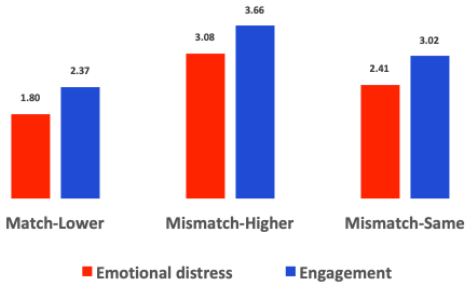


**Chart 6.22 Psychological Outcomes: Diabetes AS(Low)**

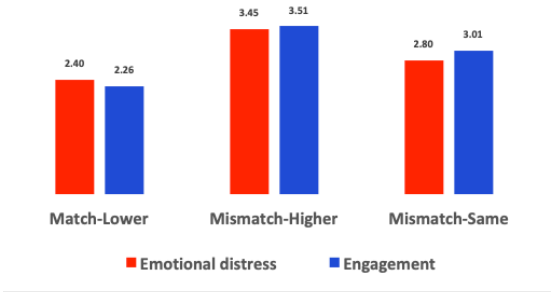


**Chart 6.23 Psychological Outcomes: Cancer AS(Low)**

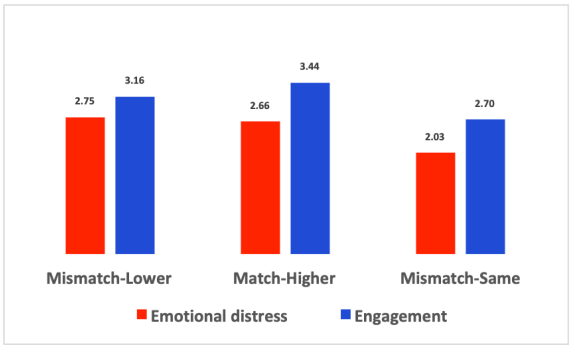


**Chart 6.24 Psychological outcomes: Diabetes AS(High)**

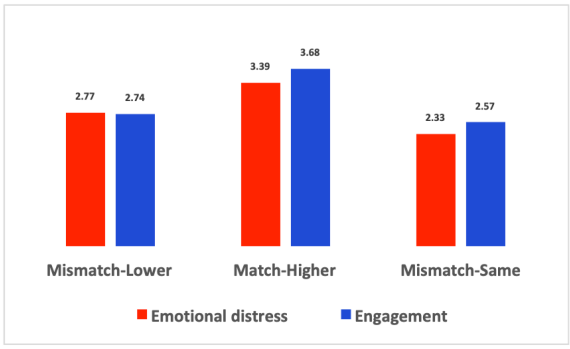


**Chart 6.25 Psychological outcomes: Cancer AS(High)**

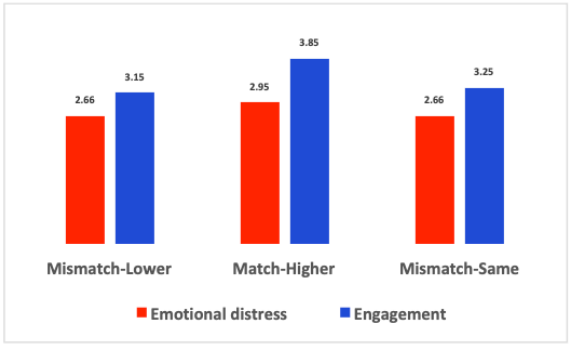


**Chart 6.26 Psychological outcomes: Diabetes AS(Higher)**

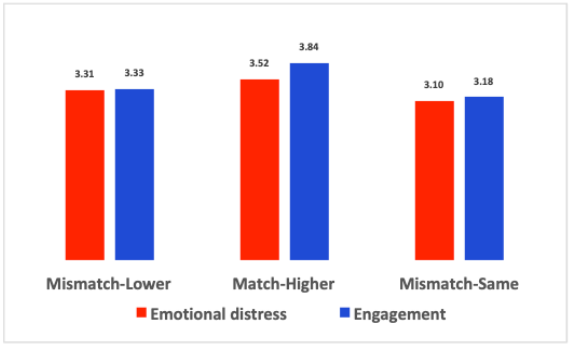


**Chart 6.27 Psychological outcomes: Cancer**

### *6.2.3 We got our results – What might we do?*

Respondents were asked to indicate their intention to engage in a suite of behaviours, such as monitoring their health more closely, if their DTCGT results were the same as the ones in each of their allocated diabetes or cancer risk treatments. For drug sensitivity, one general and one specific behavioural intention question was asked, requiring different analysis. As such, results are presented separately.

### 6.2.3.1 *Behavioural intentions: Disease predisposition tests*

Confirmatory factor analysis reduced the suite of individual behavioural intentions asked for both diabetes and cancer into five factors.[23] Intention to engage with healthcare professionals involved seeking interpretation assistance or confirmation from either doctors or genetic counsellors; share and seek information going online to share or gather additional information and find others with similar results; proactive health behaviours monitoring health and changing diet; and take no action making no decisions and not changing exercise. The final factor was intention to share with family.

*Did behavioural intention vary by country?*

For both diabetes and cancer, AU respondents expressed higher intention to engage with healthcare professionals, and lower mean intention to share and seek information, share with family, and take no action than their US counterparts (Charts 6.28 & 6.29). No inter-country differences were found for proactive health behaviours.

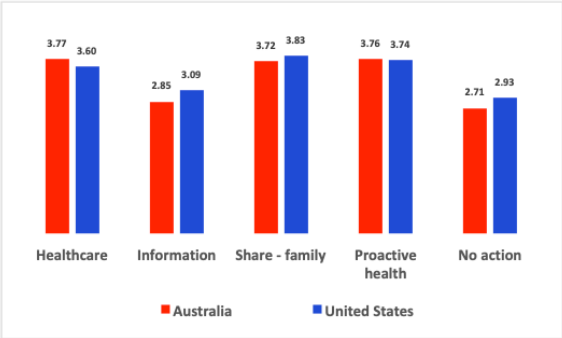


**Chart 6.28 BI (Diabetes): AU & US**

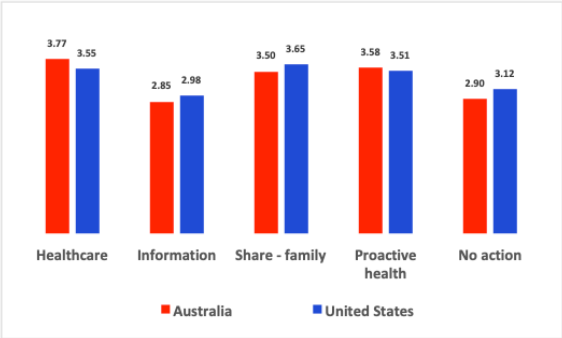


**Chart 6.29 BI (Cancer): AU & US**

At first glance, these results tend to confirm the summary of the empirical data discussed in Chapter Four. Respondents in both countries are reasonably likely to engage with healthcare professionals, engage in proactive health behaviours, especially AU respondents, and share with family, especially US respondents indicating the potential for consumer empowerment. Respondents were slightly less likely to share and seek information online or take no action, especially AU respondents. However, these results look at behavioural intention in isolation. Respondents make their behavioural intention decisions based on their interpretation of DTCGT results. The following section investigates whether these intentions were influenced by respondent interpretation of allocated results using the match/mismatch construct.

[23] See Appendix Four. As behavioural intention factors were highly correlated intra-factor but not correlated inter-factor, T-tests and ANOVA analysis were conducted rather than MANOVA analysis.

*Did behavioural intention differ by Match/mismatch?*

Behavioural intentions were analysed by each disease's match/mismatch variable: Match/mismatchD and Match/mismatchC. If there was a match relative to results interpretation (PS = AS), behavioural intentions function as de facto 'benchmarks', representing behaviours warranted by results, allowing comparisons with respondents who mismatched (PS < AS, PS > AS, PS ≈ AS). Deeming behavioural intentions as 'appropriate' and 'inappropriate' has been deliberately avoided, despite use by other researchers as indicated in Chapter Four (4.2.3), as it implicitly involves value judgements. For example, mismatching respondents intending to engage with doctors are not necessarily engaging in 'inappropriate' behaviour, as individuals with any health concerns, especially those causing psychological distress, *should* discuss them with their doctors. Rather, what should be considered is whether behavioural intentions are *warranted* based on DTCGT results, and any potential flow-on effects, such as strain on health system resources.

While actual mean scores differ, what is of note is the similar patterns between countries. For diabetes, AU respondents who mismatched expressed higher mean intention to share and seek information and take no action, as did US respondents (Chart 6.30).

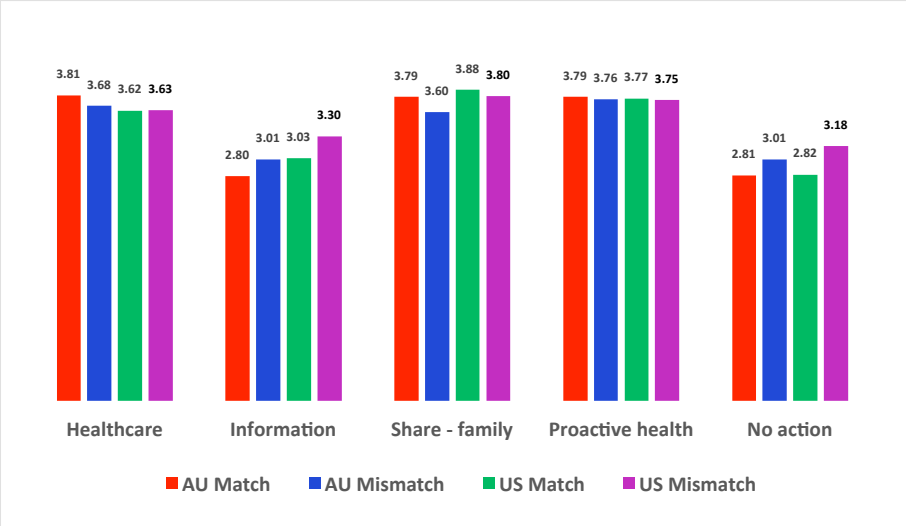


**Chart 6.30 Mean BI (Diabetes): Match/mismatch (AU & US)**

For cancer, AU respondents who mismatched expressed lower mean intention to engage with healthcare professionals and engage in proactive health behaviours, but higher mean intention to take no action, as did US respondents (Chart 6.31).

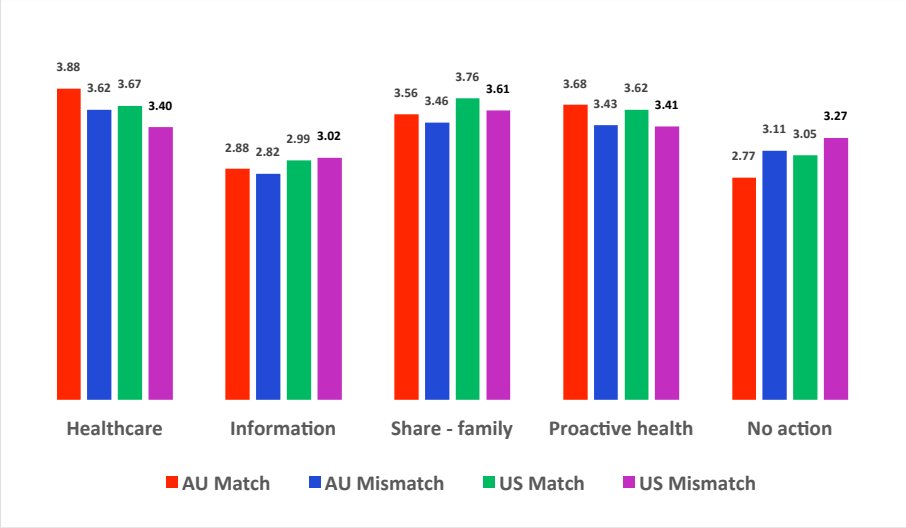


**Chart 6.31 Mean BI (Cancer): Match/mismatch (AU & US)**

The following charts allow comparison across both diseases and AS levels, with those matching in each instance representing behavioural intentions warranted by results.

For diabetes, those allocated AS(Low) who mismatched expressed higher mean intention to engage with healthcare and share/seek information but also higher mean intention to engage in proactive health behaviours than warranted by DTCGT results (Chart 6.32). For those allocated AS(High) and AS(Higher), the most notable result was the higher intention of those mismatching to take no action, with those allocated AS(Higher) also intending to seek/share information (Charts 6.33 & 6.34).

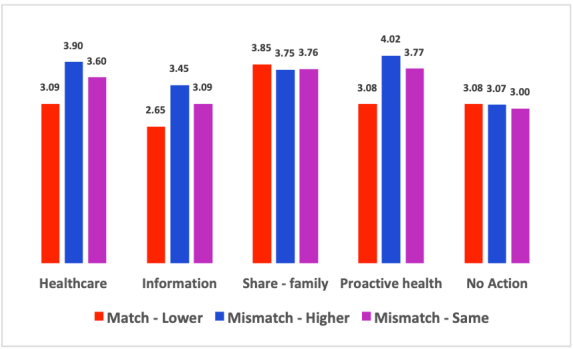


**Chart 6.32 BI (Diabetes): Low risk**

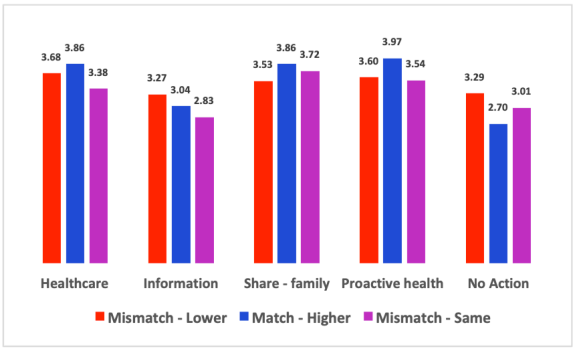


**Chart 6.33 BI (Diabetes): High risk**

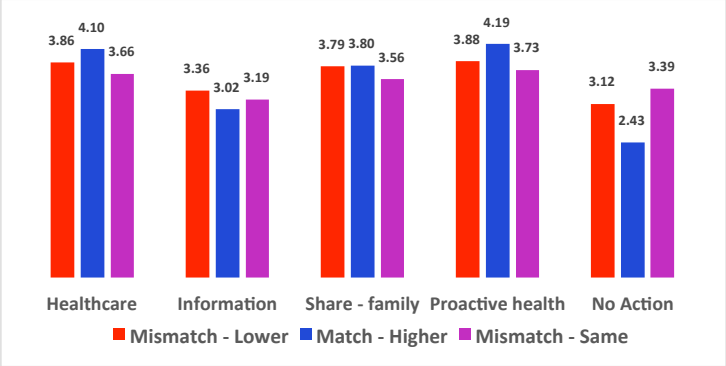


**Chart 6.34 BI (Diabetes): Higher risk**

For cancer, the same pattern was found for those allocated AS(Low), with those mismatching expressing higher mean intention to engage with healthcare and share/seek information but also higher mean intention to engage in proactive health behaviours than warranted by DTCGT results (Chart 6.35). For those allocated AS(High) and AS(Higher), the most notable result was the higher intention of those mismatching to take no action, with those allocated AS(Higher) also intending to seek/share information and share with family (Charts 6.36 & 6.37).

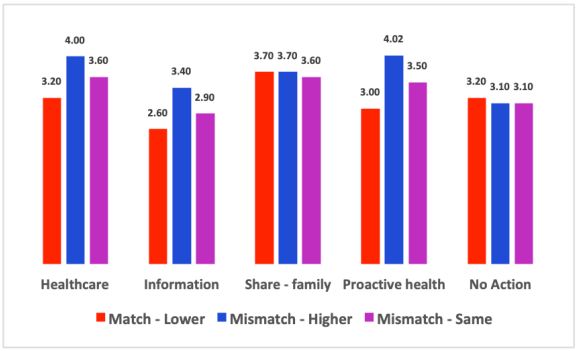


**Chart 6.35 BI (Cancer): Low risk**

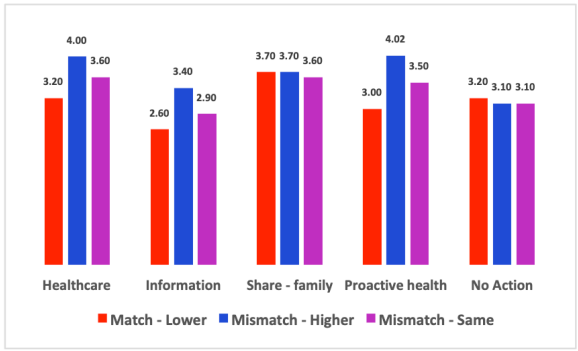


**Chart 6.36 BI (Cancer): High risk**

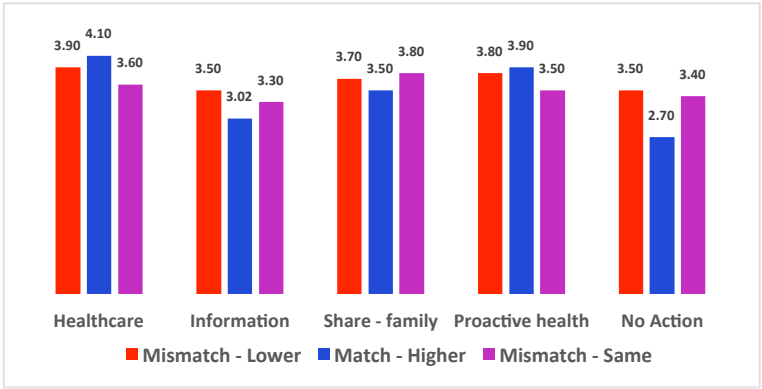


**Chart 6.37 Mean BI (Cancer): Higher risk**

Again, what is perhaps most notable from these results is the similarity of patterns between both countries and diseases. Of concern were those mismatching who were more likely to engage with healthcare when not warranted, or take no action when action was warranted by their results.

Also of concern were those mismatching who intended to share with family, as they would likely be passing on interpretation, affect and behavioural intention information not consistent with actual results. On a positive note, high mean intention to engage in proactive health behaviours was found regardless of interpretation − something the healthcare sector would certainly condone.

### *Behavioural intentionDC by Match/MismatchDC: Did interpretation affect behavioural intention overall across diseases?*

A new variable labelled Match/mismatchDC (diabetes & cancer) was created for Match/mismatch by combining Match/mismatchD (diabetes) and Match/MismatchC (cancer) scores. Combining mean scores for each diabetes behavioural intention factor with its cancer companion created new variables labelled as behavioural intention factorDC e.g. intention to engage with healthcare professionalsDC. This provides an overall indication of the impact of interpretation on behavioural intention, adjusting for specific diseases.

AU respondents who matched expressed the highest mean intention to engage with healthcare professionals while those who mismatched expressed the highest mean intention to take no action. Note the similar intention for those mismatching and inconsistent to share with family and engage in proactive health behaviours (Chart 6.38).

US respondents who mismatched expressed comparatively higher mean intention to share/seek information and take no action. Those who were inconsistent expressed higher intention to engage with healthcare, presenting a challenge to doctors who would have to distinguish consistent from inconsistent interpretations, affect and intentions (Chart 6.39).

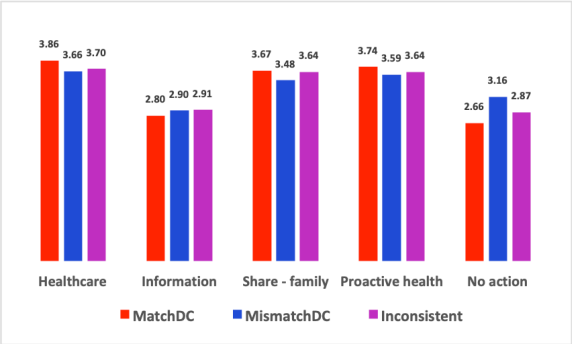


**Chart 6.38 Match/mismatchDC: BI (AU)**

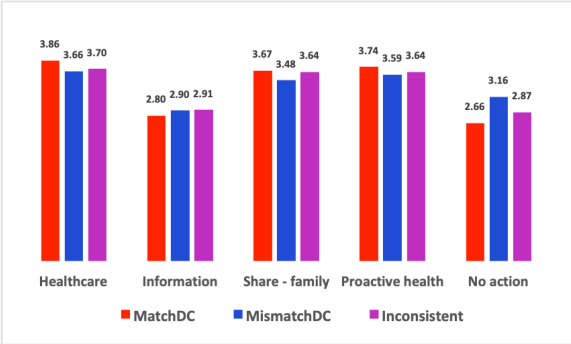


**Chart 6.39 Match/mismatchDC: BI (US)**

### *Was there a relationship between psychological outcomes and behavioural intentions?*

The preceding analysis focused on direct effects between interpretation of disease predisposition tests and psychological outcomes and behavioural intentions individually. Whether an individual

matches or mismatches at the interpretation phase has been demonstrated to have an effect on the psychological outcomes experienced and the behaviours they intend to undertake. Mismatching was been shown to individually result in disproportionate *emotional distress* and *engagement* as well as behavioural intentions not warranted by DTCGT results. One benefit of a large dataset is the ability to investigate inter-relationships to determine which might act as triggers or drivers. The following explores whether there were also relationships between the two psychological outcomes and the five behavioural intentions.[24]

For AU respondents, for both diseases, as *emotional distress* increased, so too did the Intention to engage with healthcare professionals, share and seek information, and engage in proactive health behaviours (stronger for cancer).[25] As *engagement* increased, so too did the Intention to engage with healthcare professionals (stronger for cancer), and engage in proactive health behaviours (strong for both). For cancer, as *engagement* increased, so too did the intention to share and seek, while for diabetes, the intention to take no action decreased.[26]

For US respondents, for both diseases, the same patterns were found for *emotional distress*, although notably stronger for cancer.[27] For both diseases, as *engagement* increased so too did intention to engage in proactive health behaviours (strong for both), engage with healthcare, (stronger for cancer), and share and seek information.[28]

As illustrated in Figure 6.1, what is notable is the same pattern that emerged over both diseases for both countries, although the effect was stronger for cancer. Also notable is the absence of any relationship with intention to share with family and only one negative relationship with intention to take no action.

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[24] For positive correlations, as one variable increases, so too does the other variable; as one variable decreases, so too would the other variable. For negative correlations, as one variable increases, the other decreases, and visa versa.

[25] Emotional distress with healthcare professionals (D $r$ = .382; C $r$ = .485); share and seek information (D $r$ = .342; C $r$ = .427); engage in proactive health behaviours (D $r$ = .382; C $r$ = .562).

[26] Engagement with healthcare professionals (D $r$ = .450; C $r$ = .554) and proactive health behaviours (D $r$ = .549; C $r$ = .611). Engagement with share and seek information (C $r$ = .375) and intention to take no action (D $r$ = -.298)

[27] Emotional distress with healthcare professionals (D $r$ = .487; C $r$ = .525), share and seek information ($r$ = .392; C $r$ = .425), and proactive health behaviours (D $r$ = .491; C $r$ = .525).

[28] Engagement increased with proactive health behaviours (D $r$ = .522; C $r$ = .592), healthcare professionals (D $r$ = .480; $r$ = .566), and share and seek information (D $r$ = .353; C $r$ = .353).

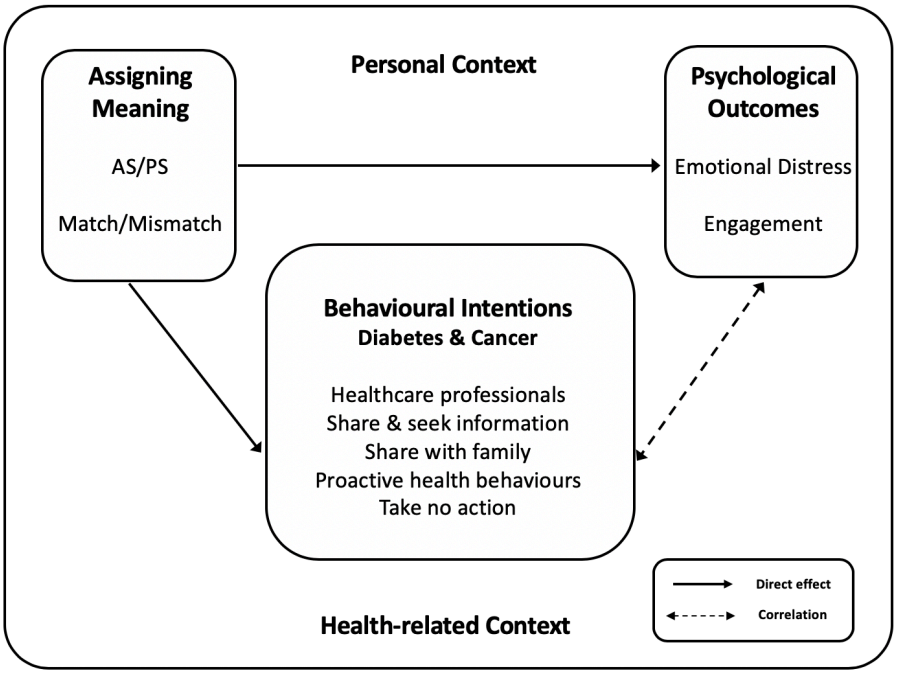


**Figure 6.1 Disease predisposition tests: Direct effects & relationships**

While interpretation was shown to have a **direct effect** on both psychological outcomes and behavioural outcomes, this analysis demonstrates the effect of interpretation on behavioural intentions may also be felt through its effect on psychological outcomes.

### *6.2.3.2 Behavioural intention – Drug sensitivity*

When asked if in general they would make decisions based on their DTCGT drug sensitivity results, approximately one-third respondents in both countries stated they would not (slow or fast metaboliser). However, the two-thirds who either would, or were uncertain, suggest DTCGT classification tests such as this one may have the potential to influence behaviour. So, might they? Respondents were asked in a separate question specifically whether they intended to change by independently increasing or decreasing dosage, make no changes, or whether they were open to changing but only after seeking expert advice.

Overall, 15% of respondents stated their intention to independently change their medication regimes (increase 7.9%; decrease 7.1%), 18% make no changes, and 67% seek expert advice. For those making no changes, DTCGT test results clearly did not have an impact. Of major concern are those who would independently change as such actions, in the absence of medical intervention, could have significant consequences. While AU respondents were much more likely to consult doctors than their US counterparts, the country effect was small (Charts 6.40 & 6.41).

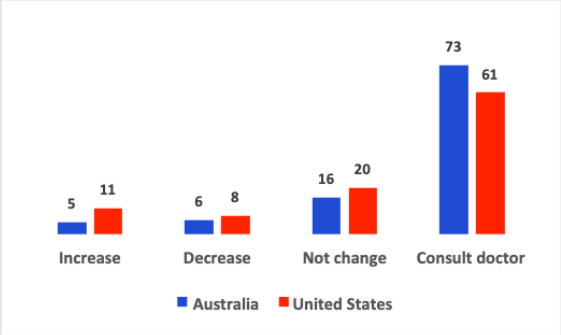


**Chart 6.40 Drug change (%): AU and US**

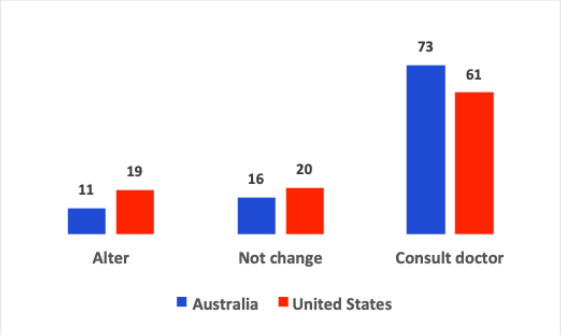


**Chart 6.41 Drug change (%): AU and US**

To put these percentages into context, although 360 respondents intended to make no change, 1340 would likely seek expert advice, representing a not insignificant strain on healthcare resources. Of primary concern, however, are the 300 individuals who would independently alter; 158 of who would increase and 142 decrease the medication regime prescribed by their doctors. Without intervention by doctors or pharmacists, these individuals could suffer potential physical or psychological harm, the effects of which may take a while to present and may be catastrophic depending on the actual medication involved and the overall medication regime. In Australia, prescribing physicians have the option to allow patients to purchase all repeat prescriptions at the time of purchasing the original prescription. Pharmacists also have discretion, and may allow purchase of all repeats at once without physician authority if, for example, the individual will be out of the country at time of refill. Of course, if particular pharmacists are not willing, individuals can always 'pharmacist shop'. As such, individuals can stockpile prescription medications, of concern for those intending to independently increase, or who choose to ignore expert advice. Stockpiling of prescriptions does not just apply to DTCGT as illustrated by the Catalyst programme and subsequent research discussed in Chapter Two (Part Two). This indicates perhaps pharmacists should play a more proactive role in terms of monitoring customers' prescriptions.

### *Did Behavioural intention differ by Psychological outcomes?*

AU and US respondents who intended to alter experienced the highest mean *emotional distress*, while those intending to consult their doctors experienced the highest mean *engagement* (Chart 6.42).

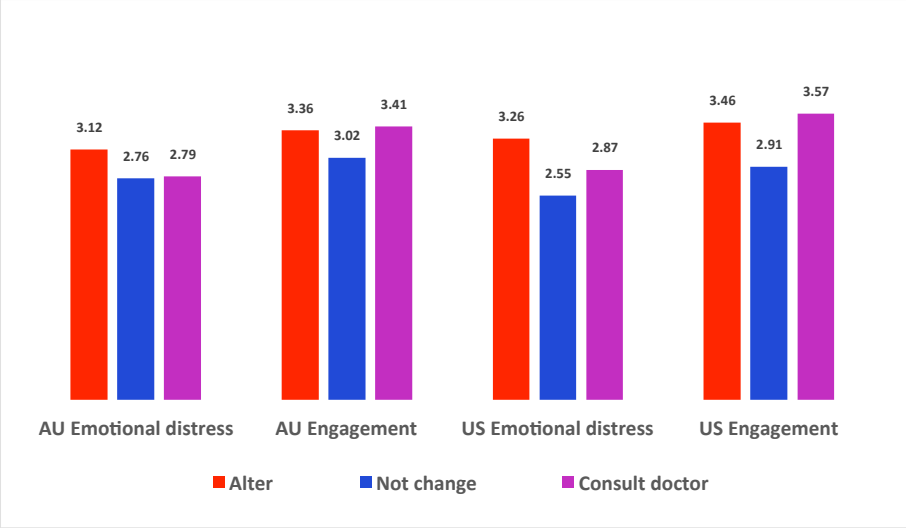


**Chart 6.42 Mean BI (Drugs): Psychological outcomes (AU & US)**

*What were the odds of altering medication regimes?*

To determine who was more likely to alter their medication regimes, either independently or with expert advice, multinomial logistic regression was conducted. When reviewed by country, US respondents were 105% (two times) *more* likely to alter rather than consult doctors compared to AU respondents.

When reviewed by respondent, while a range of effects were found, age and pills numeracy are of note, as both had large effects in both countries. As age increased, so did the likelihood of seeking expert advice. Older AU respondents were almost six times *more* likely than younger respondents to consult doctors rather than alter, and two times more likely to consult rather than not change. AU younger respondents were almost three times *more* likely to alter than not change. Older US respondents were four times *more* likely to consult rather than alter, while younger respondents were four times *more* likely to alter than not change.

Those with high pills numeracy were much more likely to seek expert advice than make independent decisions. AU respondents with high pills numeracy were three times *more* likely to not change than alter, and almost five and a half times more likely to consult than alter. US respondents with high pills numeracy were three and a half times *more* likely to not change than alter, and over five times to consult than alter.

The following relationships were found for an increase of one unit of either *emotional distress* or *engagement*. As *emotional distress* increased, AU respondents were 153% *more* likely to consult rather than alter, and 92% to consult rather than not change. US respondents were 158% *more* likely to consult rather than alter, 39% to consult rather than not change, and 85% to not change

rather than alter. As *engagement* increased, AU respondents were 109% *more* likely to alter than consult and 109% to not change than consult. US respondents were 134% *more* likely to alter than consult, and 134% to not change rather than consult.

These results suggest *emotional distress* is a key driver of seeking expert advice, consistent with high trust in doctors, while *engagement* a key driver for independent decisions, either altering or not changing.

### 6.2.4 Assessing the potential for consumer detriment

Relative to disease predisposition tests, *Perceived severity* – how an individual interprets their personal risk of developing a disease – has been shown to play a pivotal role in terms of the *emotional distress* and *engagement* they will likely experience. DTCGT genetic tests, as their name implies, only provide information about an individual's genetic *risk* of developing the disease, not the *likelihood* of them developing the disease. Determining *likelihood* requires interpretation of the genetic risk component within the context of factors such as family history, lifestyle and medical status, something individual may not do, or in fact, be capable of doing. If a mismatch occurs between the genetic risks presented in the DTCGT test results and how an individual interprets that risk, the potential exists for disproportionate levels of *emotional distress* and *engagement* – and therefore potential psychological detriment.

How individuals interpret results has also been shown to influence their behavioural intentions − how they intend to action their DTCGT results. If a mismatch occurs, the potential exists for individuals to engage in behaviours not warranted by their results, or to avoid behaviours that are warranted. While results, regardless of interpretation, appear to activate intention to engage in proactive health behaviours − a decidedly positive result − so too is the intention to engage with healthcare professionals. While this returns consumers to the medical space with the protections outlined in Chapter Three, it also represents a strain on health system resources, a system by its own admission not prepared for DTCGT. As noted, consumers presenting who mismatched or were inconsistent present particular challenges, as doctors will need to unravel inconsistent interpretations, unjustified affect and unwarranted behavioural intentions, potentially on a disease-by-disease basis. Behavioural intention is not only directly affected by interpretation but also indirectly through relationships with psychological outcomes, potentially increasing the effect of mismatching.

For the drug sensitivity results, the potential for physical or psychological harm presented depended on whether individuals intended to independently alter. While interpretation was not

explicitly tested, it is reasonable to expect the meaning individuals attached to their drug sensitivity results would implicitly lead to behavioural intention decisions.

As noted throughout Part Two, results from this research are comparable to existing empirical results discussed in Chapter Four, drawing the conclusion that *most do, some don't*. However, this research shifted the focus to those who don't match, suffer disproportional psychological outcomes and intend to engage in behaviours unwarranted by DTCGT results, as will be discussed in Part Four profiling those who mismatch – the *some* who *don't*.

# PART THREE: ASSESSING THE LIKELIHOOD OF EXPOSURE TO POTENTIAL CONSUMER DETRIMENT

Whether consumers will be exposed to any potential consumer detriment arising from either DTCGT results or the flow-on effects of sharing discussed in Chapter Four depends on their likelihood of purchase and their willingness to participate in DTCGT research. Also of interest was whether confidence in the DTCGT offering and familiarity exerted an influence.

## *6.3.1 Purchase likelihood*

Three purchase types were tested: from a company inside respondents' country of residence (purchase-inside), outside respondents' country of residence (purchase-outside), and company-initiated engagement where results were returned via consumers' doctors (results via doctor). The first two were tested at survey outset to assess general comfort with the idea of purchasing DTCGT and whether location, with its jurisdictional implications, exerted an influence. Regardless of familiarity levels or prior purchase experience, the DTCGT description at survey outset ensured a basic level of knowledge. The third was tested after exposure to the DTCGT results so could be considered as more informed. Taken together, the three purchase types also provide insight into potential consumer acceptance of different business models, important information for businesses operating in the DTCGT space, especially new entrants.

### *Did purchase likelihood differ by purchase type?*

One-way repeated measures ANOVAs were conducted, with results for both countries confirming mean purchase likelihood differed across the three purchase types, suggesting respondents viewed each as distinct (Chart 6.43). While respondents overall did not express strong purchase likelihood, AU respondents' mean likelihood was lower than their US counterparts for all three purchase types. Both AU and US expressed the highest mean purchase likelihood for results via doctor and the lowest for offshore companies.

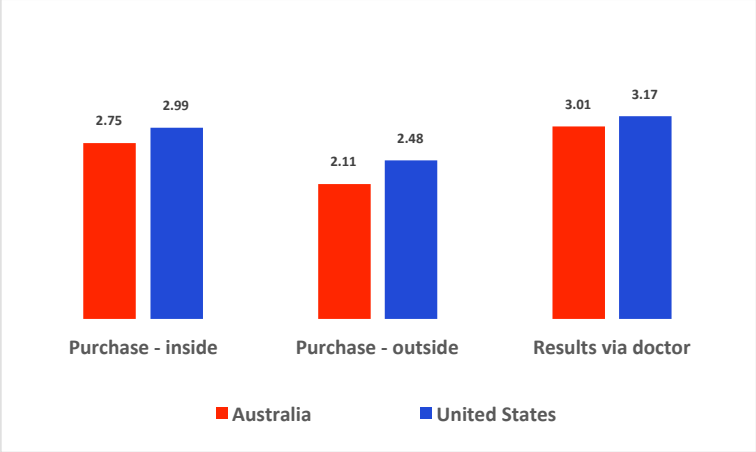


**Chart 6.43 Mean Purchase likelihood: AU & US**

Lower likelihood for offshore purchasing compared to onshore is encouraging, especially for AU respondents, given its inherent jurisdictional challenges. With onshore purchasing, AU consumers are fall under the protections outlined in Chapter Four. Higher likelihood of purchase from the company-initiated model (results via doctor) is both encouraging as it deals with the issues surrounding self-interpretation but also concerning given potential strain on the healthcare system and its lack of preparedness. Higher consumer acceptance would certainly appeal to industry, especially potential players yet to decide on business models. As illustrated in Figure 6.2, the patient-doctor relationship co-exists with the consumer-company relationship, with the individual shifting from their initial legal position as consumer to that of patient when advised by their doctor of results receipt. However, what relationship, if any, exists between the company and the doctor? Does the doctor play a passive role in this business model, accepting the wishes of their existing patient, but also accepting liability for interpretation, advice and potential actioning of DTCGT results when the consumer reverts back to being their patient? What would be the implications if doctors refuse to accept results? Do they have a professional responsibility to receive results as it involves their patients? This assumes the individual is already a patient of the doctor selected by them to receive their results. If this is not the case, even more issues are raised, including does the doctor have any responsibility to receive these 'random' DTCGT results? These significant questions will need answering if this model gains traction.[29]

[29] Ike Swetlitz, 'Genetic tests ordered by doctors race to market, while 'direct-to-consumer' tests hinge on FDA approval' *Stat*, Marcy 16, 2018 <https://statnews.com/2018/03/16/genetic-tests-fda-regulation/>.

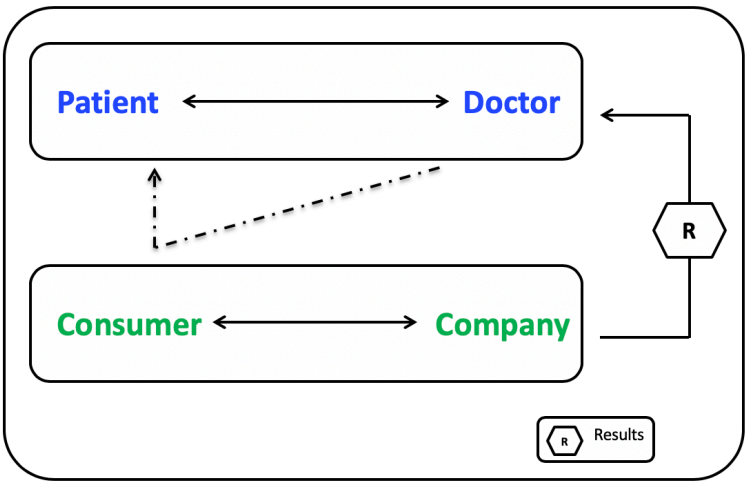


**Figure 6.2 Results via doctor**

For AU respondents, a strong relationship was found between purchasing onshore and offshore, with a moderate relationship found between purchasing offshore and results via doctor for both countries.[30] Relationships were found for both countries between familiarity and purchase both onshore and offshore, notably stronger for the US in both instances.[31] While familiarity is currently low in Australia as confirmed in this research, it is within both mass media and the DTCGT industry's power to increase through communication and marketing efforts. For purchasing offshore, similar relationships were also found for online sharing of both health and genetic information, again notably stronger for US.[32] While likelihood is low, this suggests those consumers who are likely to purchase offshore also are already comfortable sharing their information online, and would be likely to do so with genetic information obtained from offshore.

[30] Purchase-inside and purchase-outside AU $r$ = .607; purchase-outside and results via doctor AU $r$ = .408, US $r$ = .455.
[31] Familiarity and purchase-inside AU $r$ = .329, US $r$ = .574; Familiarity and purchase-outside AU $r$ = .478, US $r$ = .607.
[32] Purchase-outside and online sharing − health AU $r$ = .336, US $r$ = .499; purchase-outside and online sharing − genetic AU $r$ = .335, US $r$ = .542.

### 6.3.2 *Willingness to participate in DTCGT research*

DTCGT companies desiring access to consumer provided samples and resulting genetic data typically seek consent from consumers at the purchase stage. Issues surrounding consent, consumers becoming research participants, and monetisation of consumer genetic data discussed in Chapter Four are enlivened only if consumers are willing to participate. Respondents were asked to indicate their willingness to participate in DTCGT research after exposure the DTCGT results so can be considered as informed, regardless of initial familiarity levels. Three declared uses were tested: if genetic test information was provided to academic researchers at no cost (research-free); individuals received no personal benefit (research-no benefit), and if information was sold to another company for profit (research-profit). Providing free access DTCGT genetic databases to academic researchers and paid access to companies especially pharmaceuticals is current industry practice for the major players and is clearly outlined in contracts, as is the fact consumers will receive no personal benefit from monetisation or eventual commercialisation of research.

#### *Did willingness to participate differ by declared use?*

One-way repeated measures ANOVAs confirmed mean willingness differed by declared use for both countries, suggesting respondents viewed each declared use as discreet (Chart 6.44). While respondents overall expressed only moderate willingness, AU respondents' mean willingness was lower than their US counterparts for all declared uses. Both AU and US respondents however expressed the highest mean willingness if their information was provided for academic research at no cost, and the lowest if their information was sold for profit. While initially encouraging, each of these declared uses are bundled into DTCGT contracts that, as noted in Chapter Four (4.1.2), are generally not read by consumers. Familiarity was not found to influence research willingness, suggesting responses were based on respondents' experience with the sample DTCGT results.

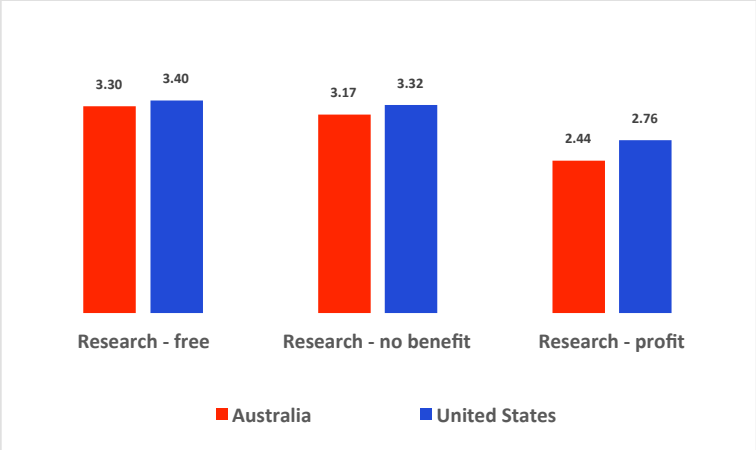


**Chart 6.44 Mean DTCGT research willingness: AU & US**

### 6.3.3 Confidence in THE DTCGT offering

Respondents were asked to assess their confidence in four aspects of the DTCGT offering identified in the literature as being of concern: sufficient information to make informed decisions (information); test accuracy (test accuracy); self-interpretation (ability to interpret); and genetic privacy (shared with permission). These questions were asked after exposure to the three DTCGT results. As respondents would all now have had experience engaging with three sets of DTCGT results, their confidence responses can be considered as informed, regardless of their initial familiarity levels.

#### *Did Confidence differ by key aspects?*

One way repeated measures ANOVA results confirmed mean scores differed for each of the four aspects in each of the countries (Chart 6.45). While respondents again did not express overly strong opinions, confidence levels did vary across the four aspects indicating respondents viewed each as distinct. In all instances, AU respondents expressed lower mean confidence than their US counterparts, with respondents from both countries expressing the lowest mean confidence in the completeness of information.

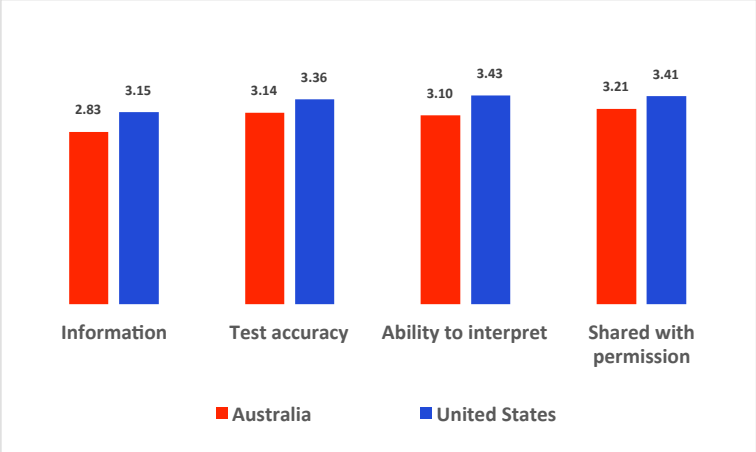


**Chart 6.45 Mean Confidence in the DTCGT offering: AU & US**

'Information sufficient to make informed decisions' provides insight into whether respondents' realised DTCGT results present genetic information only – something they certainly questioned, given lower mean scores. 'Test accuracy' represents one of DTCGT's credence qualities that cannot be evaluated either before or after purchase but must be accepted 'on trust' – something respondents, especially those from the US, appeared willing to do. 'Ability to interpret' represents a self-report measure, with US respondents definitely more confident in their own abilities than their AU counterparts. Lastly, 'shared with permission' indicates whether respondents appreciate the nature of the contractual relationships governing both DTCGT and online sharing sites. AU

respondents expressed the highest mean confidence in this aspect, with US respondents only marginally less than confidence in their own abilities. This research, and that conducted by Phillips and Charbonneau, found beliefs about companies keeping their data private do not match the reality of contract terms discussed in Chapter Four (4.1.2).[33]

Relationships were found between the different aspects for confidence in both countries, notably strong in both the relationships between information and both test accuracy and shared with permission, and test accuracy and shared with permission.[34] These latter relationships suggest, for example, the greater the confidence in the completeness of information, the greater confidence in test accuracy and genetic privacy. Familiarity was not found to influence confidence, suggesting respondents primarily determined confidence based on their experience with the sample DTCGT results.

### *6.3.4 Purchase likelihood, willingness to participate in DTCGT research and confidence in the DTCGT offering: Direct effects and relationships*

As illustrated in Figure 6.3, significant direct effects and relationships were found between purchase likelihood, willingness to participate, and confidence for both AU and US. While relationships are noted from the perspective of one variable, relationships work both ways.

[33] Andelka Phillips and Jan Charbonneau, 'Giving away more than your genome sequence?: Privacy in the Direct-to-Consumer Genetic Testing Space', (2016) Presentation at PrivacyCon, Federal Trade Commission, Washington <https://www.ftc.gov/system/files/documents/public_comments/2015/10/00057-98101.pdf>.
[34] Confidence-information and test accuracy AU $r$ = .567, US $r$ = .612; ability to interpret AU $r$ = .408, US $r$ = .490; shared with permission AU $r$ = .497, US $r$ = .525; Confidence-test accuracy and ability to interpret AU $r$ = .406, US $r$ = .512; shared with permission AU $r$ = .542, US $r$ = .606; Confidence-ability to interpret and shared with permission AU $r$ = .331, US $r$ = .443.

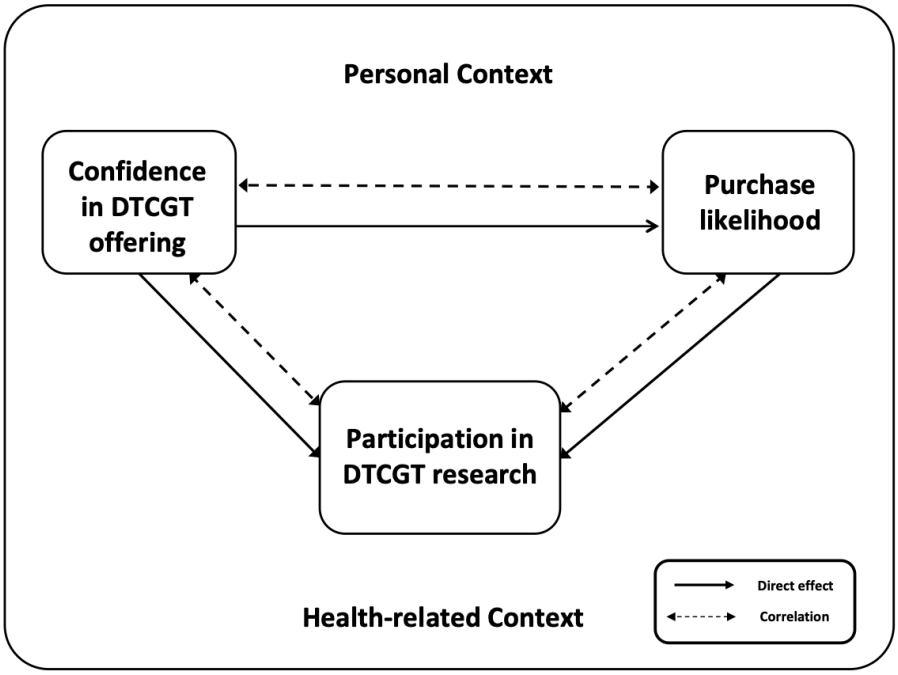


**Figure 6.3 DTCGT: Direct effects and relationships**

Confidence in the DTCGT offering was found to have a **direct effect** on purchase likelihood in both countries, although actual effects varied. AU and US respondents likely to purchase if *onshore* or *return via doctor* expressed the highest mean confidence in all four aspects. US respondents likely to purchase *offshore* also expressed the highest mean confidence in all four aspects, while AU respondents expressed more confidence in information and test accuracy. Confidence in information and test accuracy are consistent *drivers* of purchase likelihood across purchase types.

Purchase likelihood was found to have a **direct effect** on research willingness, although again actual effects varied. AU respondents willing to participate if data provided at no cost exhibited the highest mean likelihood of purchasing from an *onshore* company, while US respondents were willing relative to the three purchase types. AU and US respondents willing to participate even though no personal benefit or if data was sold for a profit exhibited the highest mean likelihood of purchase of the three purchase types.

Respondent confidence in the DTCGT offering also had a **direct effect** on willingness to participate in DTCGT research. AU and US respondents willing to participate for the three declared uses expressed the highest mean confidence in the four aspects. Confidence therefore represents a key **driver**, having a **direct effect** individually on purchase likelihood and research willingness but also an effect on research willingness through its effect on purchase likelihood.

Relationships were found between purchase likelihood if results were returned via doctor and confidence in test accuracy for both countries, but no consistent relationships were identified for the other purchase types.[35] For both countries, relationships were found between willingness to participate in research if provided at no cost and confidence in information, test accuracy and shared with permission, as well as purchase likelihood if results returned via doctors.[36] The relationship was notably stronger in both countries for confidence their information would only be shared with their permission: as such, the more confident respondents were in their genetic privacy, the more willing they were to participate in the research. These same relationships were also found for willingness to participate in research even if no benefit in both countries, with confidence in genetic privacy again being notably stronger.[37] Relationships were also found for AU and US between willingness to participate if sold for profit and confidence in information, test accuracy and genetic privacy as well as offshore purchase likelihood.[38] Taken together, these relationships highlight the overall importance of confidence in the DTCGT offering.

Overall, relationships found were stronger for the US with two exceptions. The relationship between confidence in test accuracy and data shared with permission and willingness to participate with no personal benefit was stronger for AU.

### *6.3.5 Assessing the potential for exposure to consumer detriment*

As overall purchase likelihood was relatively low, especially for AU, the likelihood of exposure to consumer detriment would also be generally low for *most*... but what about the *some*. Results discussed in Part Three have indicated those more confident in the DTCGT offering would be more likely to purchase and would also likely consent for their genetic data to be used in DTCGT research. Results discussed in Part Two indicated those who mismatch at the interpretation stage were likely to experience unjustified psychological outcomes and intend to engage in unwarranted behaviours. Looking at this group − the *some* − as actual numbers of individuals presents a clearer picture. As illustrated in Table 6.4, out of the 2000 respondents surveyed, 576 stated they were likely to purchase from an onshore company, 330 from an offshore company, and 756 if results were returned via their doctors. Those likely to purchase from onshore or

[35] Results via doctor and test accuracy AU $r$ = .300, US $r$ = .366.
[36] Research − free and information AU $r$ = .302, US $r$ = .397; test accuracy AU $r$ = .429, US $r$ = .474; shared with permission AU $r$ = .504, US $r$ = .511; results via doctor AU $r$ = .301, US $r$ = .328.
[37] Research no benefit and information AU $r$ = .377, US $r$ = .424; test accuracy AU $r$ = .495, US $r$ = .461; shared with permission AU $r$ = .529, US $r$ = .498; results via doctor AU $r$ = .326, US $r$ = .350.
[38] Research profit and information AU $r$ = .398, US = .528; test accuracy AU $r$ = .366, US $r$ = .437; shared with permission AU $r$ = .359, US $r$ = .406; purchase − outside AU $r$ = .316, US $r$ = .387.

offshore companies will likely be exposed to consumer detriment *IF* they mismatch. The larger proportion likely to purchase from onshore will at least be afforded the protections outlined in Chapter Three.

Returning results via doctors shifts interpretation, advice and actioning back to the healthcare system thereby, at least in theory, negating *consumer* detriment. However, by its own admission the system is not prepared so the risk of inconsistent interpretation, unjustified affect and unwarranted behavioural intentions, while reduced, is not totally negated, theoretically generating the potential for *patient* detriment. Doctors would also be faced with the challenge of 'untangling' results for those who were inconsistent in their interpretations, matching for some and mismatching for other DTCGT results.

**Table 6.6 Respondents likely to purchase: Three purchase types**

| **Respondents** | **Purchase likelihood** | | |
|---|---|---|---|
| | AU | US | Overall |
| *Purchase – inside* | 218 (21.8%) | 358 (35.8%) | 576 (28.8%) |
| *Purchase – outside* | 92 (9.2%) | 238 (23.8%) | 330 (16.5%) |
| *Results via doctors* | 342 (34.2%) | 414 (41.4%) | 756 (37.8%) |

% of the sample for each purchase type

## PART FOUR: SHIFTING THE FOCUS FROM THE *MOST* TO THE *SOME*

Results discussed in Part Two found those who mismatched at the interpretation stage were more likely to experience unjustified psychological outcomes and to intend to engage in unwarranted behaviours than those who matched. While the percentage mismatching was decidedly smaller than those matching, the actual number of individuals mismatching is cause for concern, deserving of a closer look. Those who mismatched were looked at first by disease and then overall to adjust out disease and country differences.

### *6.4.1 Did mismatch differ by disease?*

Younger respondents were much more likely to mismatch but only for diabetes. For both diabetes and cancer, those with low risk and pills numeracy, and those who had purchased were much more likely to mismatch, although effects were all small. Lower health numeracy resulting in increased likelihood of mismatching is understandable. However why respondents with purchase experience mismatched is less clear, and may simply be the results of the lower numbers with experience, especially for AU.

Those who mismatched for the diabetes test results expressed lower mean health active and higher mean health passive scores; lower mean understanding of the diabetes results; lower mean trust in doctors and higher mean trust in health communities; higher mean frequency of self-diagnosis and online sharing of both health and genetic information; higher mean familiarity; higher mean confidence in the sufficiency of information; higher mean likelihood of offshore purchase; and higher mean willingness for research sold for profit. Taken together, this paints a picture of respondents less engaged with traditional aspects of healthcare such as lower trust in doctors and health active scores; but more engaged with online aspects of healthcare such as self-diagnosis.

Interestingly, fewer commonalities were found for cancer, with those who mismatched expressing higher mean health passive scores; lower mean understanding of the cancer results; lower mean trust in doctors; higher mean frequency of online sharing – genetic; and higher mean likelihood of offshore purchase. While only two disease predisposition tests were analysed, these results support concerns expressed in the literature relative to bundling of DTCGT tests.

### *6.4.2 Did mismatch differ by other factors?*

Those with low risk numeracy were much more likely to mismatch while those with low pills numeracy and had purchase experience were much more likely to mismatch or be inconsistent. However, again effects were small.

Those who mismatched exhibited lower health active and higher health passive scores; lower mean trust in doctors; higher mean frequency of self-diagnosing and online sharing of both health and genetic information; higher mean familiarity; higher mean likelihood of purchase-outside; and higher mean willingness to participate if data sold for profit.[39]

When viewed from the perspective of commonalities found for those mismatching when compared to those who matched, a slightly more focused picture emerges. Both risk and pills numeracy had a greater effect on interpretation than previous analysis indicated, as did test purchase experience. The latter result, while approached with caution, is nonetheless interesting as purchasers have at least some experience interpreting genetic tests, albeit not necessarily DTCGT.

[39] Scores for those inconsistent were consistently between those for who matched or mismatched as they had either matched, mismatched or were unsure for one disease.

Relative to disease predisposition tests, self-report understanding, passive involvement in health, regular sharing of genetic information and lower trust in doctors also had a greater effect on interpretation than previously demonstrated. This indicates the health-related context (skills, attitudes and behaviours) that individuals bring to DTCGT engagement has an impact, warranting further investigation.

Of concern relative to the two diseases and overall was the greater likelihood of purchase from offshore companies where expected protections may not apply due to jurisdictional differences. As such, even if consumer detriment is both in evidence and acknowledged by individuals, recourse may not be available. What is also of note are the comparatively small number of commonalities found given the large range of variables analysed, making identification of potentially vulnerable consumers pre-test extremely difficult.

## PART FIVE: STRENGTHS AND LIMITATIONS

This survey, as all surveys, had both strengths and limitations. Data was collected contemporaneously from robust samples in two countries representing sub-strata of their general publics − Internet-literate individuals. The majority were not early adopters as was the case with much of the existing empirical research and, as such, represented potential consumers currently being targeted by DTCGT companies. The survey itself investigated significant aspects of the DTCGT process, from familiarity and purchase likelihood, through interpretation, affect and behavioural intentions, confidence in the offering, to willingness to participate in company research, allowing in-depth exploration of relationships. The survey also collected data relative to a range of personal characteristics, health status and health-related skills, attitudes and behaviours, providing insight into the context within which individuals engage with DTCGT. Embedded into the survey were robust experiments, all rigorously pre-tested. Quotas ensured gender and age representation as well as equal distribution across the experimental design. Conservative interpretation sought to control for Type I errors (false positives), with robust analysis conducted to identify substantive and meaningful patterns and relationships.

However, as with all surveys, data collected was self-report from individuals who self-selected to participate, and responded to fixed choice questions. That respondents answered honestly, reflecting their actual opinions, was accepted 'on faith'. While all due care was taken during analysis, the potential for errors and omissions always exists, especially with such a large dataset and a nascent statistician. No claims can be made as to generalisability and the survey's lack of ethnic diversity has to be acknowledged. The survey's largest limitation is that it was conducted

with *potential* consumers evaluating *hypothetical* results and indicating behavioural *intentions* only – not actual consumers evaluating their own results and reporting actual behaviours.

That being said, opportunities abound for future research, for example in other countries or with particular groups of interest such as older consumers. The focus of this analysis was primarily on broad patterns, the dataset represents a treasure trove of nuanced detail to be explored.

## CONCLUSION

When viewed holistically, focusing on broad patterns rather than nuanced detail, the following picture emerged from the data. Purchase likelihood represents a key variable. Simply stated, without purchase, individuals are not in possession of DTCGT results needing interpretation, or genetic information that may be shared, and therefore not exposed to any potential consumer detriment. However, should purchase occur, individuals are faced with interpreting complex DTCGT results, experiencing resultant affect, and making decisions as to actioning, potentially being exposed to consumer detriment. Individuals also decide whether to share results with family, their doctors, online or allow DTCGT companies to use their data, potentially exposing them, for example, to privacy breaches.

Confidence in the DTCGT offering has been demonstrated in this research to have both direct and indirect effects on purchase likelihood and willingness to participate in DTCGT company research. Purchase likelihood was also demonstrated to have both direct and indirect effects on research willingness (Figure 6.3). Simply stated, the more confident individuals are in the information provided, test accuracy, their own interpretation abilities, and whether their information would only be shared with permission, the more likely they are to purchase and allow DTCGT companies to use their data. While purchase likelihood is currently low, especially in Australia's emergent market, forecasts discussed in Chapter Two (2.3.3) suggest increased uptake over the coming years. It must also be noted that confidence in the DTCGT offering can be increased through company communication efforts and public-wide genetics education.

For those purchasing, this research has demonstrated the pivotal role played by interpretation. How individuals interpret DTCGT results has been shown to have a **direct effect** on psychological outcomes and behavioural intentions, and a *mediated effect* through the relationship between psychological outcomes and behavioural intentions (Figure 6.1). If interpretation is consistent with actual DTCGT results (match), individuals experience psychological outcomes justified by, and state intentions to engage in behaviours warranted by, their results. However, should

interpretation be inconsistent (mismatch), individuals experience unjustified psychological outcomes (greater or lesser) and intend to engage in behaviours not warranted by their results. Results have further shown that interpretation may vary depending on the type of test or disease, a concern given the bundled nature of the DTCGT offering.

When offered the option to engage with healthcare, respondents took it, either consumer-initiated seeking assistance and actioning of DTCGT results or company-initiated where purchase likelihood was highest if results were returned via doctors. This was especially so for AU respondents, perhaps because of the universal coverage of AU's healthcare system or high trust in doctors. As discussed in both Chapters Three and Four, this engagement has both cost and preparedness implications that will need to be addressed if DTCGT uptake increases.

As detailed in Chapter Five Part One, the survey component of this research sought to answer five research questions. These research questions have been answered as follows. There *IS* potential for psychological detriment through false reassurance or unjustified distress *IF* consumers mismatch at the interpretation stage (*Research question one*). Consumers *WILL* be exposed to potential psychological detriment *IF* they purchase, and then mismatch (*Research question two*). DTCGT results *DO* motivate behavioural intention to change, but these intentions may be unwarranted *IF* they mismatch (*Research question three*). Whether such behavioural intention will actually result in behavioural change, let alone sustainable change, is not known, leaving the question of potential consumer empowerment unanswered. DTCGT results *DO* motivate intention to engage with healthcare, although again, this may be either unwarranted or actively avoided *IF* they mismatch (*Research question four*).

What was perhaps most striking about the results was the similarity between AU and US respondents, especially relative to interpretation, affect and behavioural intention. It was noted US respondents generally expressed stronger opinions − both positive and negative − and were influenced by more personal and health-related contextual factors than their AU counterparts, although this influence was not itself consistent. However, when data charts were reviewed, the similar patterns became apparent, although actual numbers or intensity often differed.

The lack of consistent, substantial differences inter-respondent means it would be difficult to identify pre-test which consumers might be susceptible and therefore vulnerable to potential consumer detriment (*Research question five*). It would also be difficult to identify post-test those who mismatch, as individuals themselves who would need to first determine they had mismatched, assess the implications of mismatching, and then bring it to the attention of

regulators. The traditional 'adverse incident' approach to enlivening the attention of either the medical or consumer sphere is unlikely to occur in the context of DTCGT. This is especially so in Australia where all pharmaceutical and medical interventions are firmly within the medical sphere. Engaging with healthcare, either consumer or company-initiated *may* ultimately prove to be beneficial overall, especially to the psychological health of DTCGT consumers, assuming the sector is prepared to interpret and action DTCGT results. However, it would be remiss to not note the potential for harm, especially psychological, also exists with CGT – the presence of a healthcare provider does not eliminate the possibility for misunderstanding, unjustified affect and unwarranted behavioural intention.

DTCGT companies provide bundled test results in template form to all consumers. This allows for the most efficient processing of results, with the limited personalisation avoiding anything resembling a diagnosis or advice that might expose them to potential unauthorised practice of medicine, as suggested by critics, and increased liability.[40] Clearly the results of this survey suggest that, while this 'one size' approach fits *MOST*, it does not fit *ALL*. Determining what alterations are needed is unclear given the lack of consistent, substantial inter-respondent differences. It is also clear the industry's aim to provide no ambiguity has not been fully achieved − and may even turn out to be unachievable.

This chapter has demonstrated the potential for *personal non-financial hidden* detriment exists in the DTCGT offering. However, the Consumer Policy Toolkit discussed in Chapter Three (3.6.1) does not specify the quantum of detriment required to prompt regulatory action. The key question remains whether it is of sufficient concern to prompt action from Australian regulators, to be addressed in Chapter Seven.

[40] Jennifer Wagner, 'Interpreting the Implications of DNA Ancestry Tests' (2010) 53(2) *Perspectives in Biology and Medicine* 231-248; Andrew Pollack, 'Gene testing questioned by regulators' *New York Times*, 26 June 2008.

# Chapter Seven:

# Break down the silos – or limp further and further behind

*'Law, marching with medicine but in the rear and limping a little'*

Justice Windeyer

# INTRODUCTION

While Justice Windeyer of the High Court of Australia was referring in the opening quote to negligence for nervous shock in the 1970 case of *Mount Isa Mines Ltd v Pusey*, well before the completion of the Human Genome Project in 2003, add science and technology to medicine, and the quote still has resonance today.[1] Law, by its very nature advances slowly in a generally reactive rather than proactive manner.[2] Science and technology, especially in genetics, moves fast and at a rapidly accelerating pace in today's intensely competitive commercial space. As 'the brave new world' envisioned by Francis Collins in the context of personalised medicine becomes the norm, demand from patients, medical professionals, and consumers for clinical or market translation of the latest genetic research will only increase creating pressure especially on the over-burdened health system. Given limited health system resources, perhaps DTCGT can act as a temporary safety valve, releasing some of this pressure. And the emergence of new business models in the DTCGT sector may well 'usher in new collaborations between patients, consumers, medical providers, and regulators that maximize the benefits of genetic information, through the empowerment of patients and providers.'[3]

This concluding chapter is organised into three parts. Part One recaps the findings of the preceding six chapters that sought to determine 'where we are' currently relative to DTCGT – a critical requirement before deciding which, if any, 'regulatory road' to pursue, to paraphrase the Lewis Carroll quote from Chapter One. Applying both legal and consumer behaviour lenses identified the possibility for individuals to assume the roles of *consumer, patient* and *research participant*, each in different regulatory spaces, each afforded different legal protections. Survey results determined that the potential for consumer detriment does exist when individuals engage with DTCGT; the pivotal role played by results interpretation; and the high likelihood of engagement with the healthcare system, with its cost and expertise implications.

Part Two provides an overview the recommendations that have been made as to regulating DTCGT and requirements for effective regulation. Recommendations were made from a range of disciplines, each applying their own lens, and each focusing on specific regulatory spaces and

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[1] *Mount Isa Mines Ltd v Pusey* (1970) 125 CLR 383 at 395.
[2] See James Farrell, ' Slow, expensive, complicated legal system must be improved' *The Conversation* April 10, 2014 <http://theconversation.com/slow-expensive-complicated-legal-system-must-be-improved-25382>; Rosalind Croucher, 'A window on law reform for government lawyers', *Australian Law Reform Commission* August 28, 2012 <https://www.alrc.gov.au/news-media/2011-2012/window-law-reform-government-lawyers>.
[3] Megan Allyse, David Robinson, Matthew Ferber and Richard Sharp, 'Direct-to-consumer testing 2.0: Emerging models of direct-to-consumer genetic testing' (2018) 93(1) *Mayo Clin Proc* 113-120, 120.

aspects of DTCGT. While each had merit, taken together they do not provide consistent guidance to regulators.

Part Three reviews how regulations in the three identified regulatory spaces – medico-legal, consumer and research – have resulted in 'regulatory congestion'. Deciding which 'regulatory road' to pursue, if any, first requires navigation of this 'regulatory congestion'.[4] The overarching recommendation of this research is discussed, suggesting there is not a need for *more* law but rather the *right* law, one 'fit for purpose', requiring input and cooperation from the three regulatory spaces. Genetics education for both the healthcare sector and general public is needed regardless of regulatory action.

## PART ONE: RECAPPING 'WHERE WE ARE'

This research sought to shine a light on the DTCGT industry by applying both law and consumer behaviour lenses and using a combination of doctrinal analysis, modelling of both the DTCGT and CGT spaces, and empirical data collected in survey experimentation focusing on potential consumers engaging with hypothetical DTCGT results.

### *7.1.1 The complex mix of genetics, environment and chance*

To understand either CGT or DTCGT information and interpret results provided by DTCGT companies, individuals must have at least a basic understanding of genetics and the role it plays in inheritance and disease. Even the basic overview of genetics provided in Chapter Two illustrates the complexity of the *Book of Life* that determines who YOU are and will become. And that is before genetic interaction with environmental factors or the whims of Lady Luck (chance) are added in. DTCGT consumers must understand that DTCGT results provide genetic information only, usually based on small genetic variations (SNPs) that the 'science of the day' indicates are associated with particular diseases. Most of the SNPs used are only weakly associated, requiring interaction with other, both known and unknown, genetic and environmental factors for diseases to present. Most DTCGT results present predisposition information only – the personal risk that diseases may present compared to the average person's risk. Even though an individual's genetic risk may be higher than average, this does not mean they will definitely develop the disease. Significantly, risk mitigation strategies such as lifestyle changes often exist. Equally individuals need to recognise DTCGT results provide no information about onset, symptoms or their severity.

[4] See Graeme Laurie, 'Liminality and the limits of law in health research regulation: What are we missing in the spaces in-between' (2016) 25(1) *Medical Law Review* 47-72

### 7.1.2 The business of genetics

In the mid 19th century as Darwin developed his theory of evolution and Mendel conducted his pea experiments, neither could not have imagined their work would lead to diagnosing and, perhaps, eventually eradicating human diseases. Since that time, science and technology have developed a symbiotic relationship with commercialisation creating the necessary environment for DTCGT to gain a profitable foothold. Commercialisation in genetics is not new and will continue, and indeed must continue, as such commercialisation plays a significant role in translating genetic discoveries, coupled with technological advances, into genetic tests and treatments with the potential to both enhance and extend life quantity and quality. The Human Genome Project served to highlight the growing tension between public science and commercial science and the speed at which the commercial sector operated and its clear intention to monetise its discoveries. The business of genetics has proven lucrative, especially when afforded patent protection, and accelerating rates of genetic discoveries and technological advances will only intensify the commercial imperative to monetise and whet the general public's desire to benefit.

### 7.1.3 DTCGT's disruptive nature: Destined to create controversy

DTCGT represents a disruptive innovation that challenges the traditional paradigm of CGT and, as such, was always going to create controversy. While genetics commercialisation is necessary to support CGT development, DTCGT challenges the medical community's exclusive purview over genetic testing, by providing individuals with a genetic testing option available not in the clinic under the control of medical professionals but in the marketplace under their own control. DTCGT's key promise is consumer empowerment − that individuals armed with their own personal genetic information can take an active role in their own health and healthcare. While the promise itself is certainly appealing, as DTCGT companies gained traction in the international marketplace, fuelled by increased Internet penetration and consumer acceptance of e-commerce, attention shifted to critically evaluating the likelihood this promise of consumer empowerment would eventuate. Much of this critical evaluation focused on the potential for consumers to suffer harm, especially psychological, when engaging with DTCGT given self-interpretation, and whether the genetic information presented would actually prompt consumers to engage in proactive and sustainable health behaviours. Also of concern was the speed with which the DTCGT sector added tests to its bundled offering, suggesting the potential for premature translation of today's science that may be proven less reliable or even erroneous tomorrow.

### 7.1.4 The DTCGT space: Consumers, patients and research participants

Before addressing whether existing regulation is sufficient or if reform is needed, a solid understanding of the space to be regulated was required. Prior to the advent of DTCGT, genetic testing was only obtainable within the Australian healthcare system where access was tightly controlled, funding was based on test validity with an emphasis on clinical utility, and results were expertly interpreted and actioned. DTCGT offered individuals seeking genetic information, for whatever reason, an alternative, available to anyone willing to spit and pay, representing a paradigm shift from medical to consumer. Modelling of both the CGT and DTCGT spaces in Chapter Three illustrated these two pathways afforded individuals different protections, enlivened by whether they obtained genetic results as a *patient* or received results as a *consumer*. Analysis of processes on both an individual and sector-basis highlighted significant differences. When engaging with DTCGT, consumers perform their own needs assessment, agree to be governed by company-specific terms and privacy policies, and receive results requiring them to both interpret and implement − expert advice is not typically part of the process. In stark contrast, with CGT, needs assessment entails expert determination of personal clinical relevance of each test, with results interpreted and possible treatments or interventions investigated before presentation to patients − all of which require informed consent. Expert advice, including that provided to patients by genetic counsellors, is available at each step, as and when needed.

In-depth analysis of the CGT and DTCGT spaces in Chapter Three identified that the initial bifurcated system of pathways − consumer *or* patient − could merge or intersect either as the result of company-initiated or consumer-initiated engagement with healthcare − with individuals both consumers and patients. This analysis also identified the flow-on effects on both privacy and potential monetisation of sharing genetic information with family, online, and by agreeing for DTCGT-generated genetic data to be used in company research. The latter introduced the new role of *research participant* − meaning an individual engaging with DTCGT could be a consumer, patient *and* research participant.

Key medical, quality and financial gatekeepers involved in the CGT process each provide protection for Australian patients by ensuring genetic tests offered are valid and samples properly analysed, only tests with clinical utility are subsidised, and all involved in the process meet the highest of professional standards. The designation of *patient* enlivens a host of legal protections against, for example, medical negligence. The designation of *consumer* as applicable to DTCGT also enlivens particular legal protections, principally those contained in the Australian Consumer

Law (ACL). The Consumer Policy Toolkit provided guidance for determining whether specific consumer protection is needed for DTCGT consumers, with its focus on determining and quantifying consumer detriment. While CGT protections are firmly within Australian jurisdiction, given DTCGT's typically online business models, Australian consumers are only guaranteed protection if purchased from companies within Australia's jurisdiction.

### *7.1.5 DTCGT concerns: Looking for 'monsters under the bed'*

As the volume of academic literature, position statements from genetics-related organisations and government reports increased, key themes have emerged relative to concerns being advanced. While not exhaustive, three illustrative themes were identified and developed in Chapter Four: concerns about the DTCGT offering; concerns about DTCGT's impact on the individual; and concerns about its impact on healthcare systems. Concerns with the offering focused on the validity of DTCGTs and the potential for error when thousands of SNPs are analysed. DTCGT companies generally offer a bundle of tests rather than providing consumers with options. As such, any validity or error issues could conceivably be multiplied. Also identified were issues with the contracts that governed consumers' interaction with DTCGT companies. Of particular concern were waiver of property rights and no benefit sharing clauses that effectively provided companies the right to both use and monetise resultant consumer genetic data. A key concern was whether informed consent was obtained when consumers mouse-clicked their contractual agreement. Questions were also raised about DTCGT marketing activities and whether the primary focus on benefits at the expense of limitations allowed consumers to make informed purchase decisions.

Concerns about how DTCGT impacts on the individual questioned how individuals interpret results, how they feel after interpreting and what they might do with the information. The potential for unjustified anxiety from false positive results and false reassurance from false negative results and whether test results encourage behavioural change were particularly highlighted. Concerns were also identified as to the sharing of genetic information with family and online, especially if there were issues with interpretation, or as part of DTCGT company research. With the latter, much of the concern centred on whether informed consent was obtained and whether individuals were adequately protected as research participants. Results of DTCGT empirical research, mainly conducted with early adopters in the US, suggested most individuals consistently interpreted results, suggesting limited cause for concern. However, the fact most actual customers did not engage in sustainable behavioural change suggested limited optimism relative to delivering the DTCGT industry's key promise of consumer empowerment.

Many commentators have suggested consumers, especially those confused with or overwhelmed by DTCGT results, would rely on the healthcare system for interpretation assistance and advice. Whether consumer or company-initiated, such reliance would not be cost-neutral, further stretching already limited health system resources. And, by their own admission, healthcare professionals are not prepared, either in terms of expertise or resources. In Australia's healthcare system, DTCGT consumers seeking pharmaceutical or medical interventions based on their DTCGT results, regardless of interpretation, have no option but to turn to the healthcare system.

### *7.1.6 Potential consumers engage with sample DTCGT results: What the survey found*

Results of the modelling exercise in Chapter Three coupled with the concerns articulated in Chapter Four provided guidance for the survey component of this research. The methodology for the survey was reported in Chapter Five and the results were reported in Chapter Six. This empirical evidence-based component explored potential consumer detriment, especially psychological detriment. Analysis of responses from 2000 Australian and American respondents to an online panel survey with embedded experimentation revealed that interpretation inconsistent with DTCGT risk information presented for diabetes and cancer resulted in disproportionate levels of *emotional distress* and *engagement* and intentions to engage in behaviours not warranted by results. The 'match/mismatch' construct was developed based on whether interpretation was consistent with actual results presented. Analysing results through the lens of 'match/mismatch' revealed while *most* respondents' interpretation was consistent, psychological outcomes justified and behavioural intentions warranted, however for *some* the potential for consumer detriment was found. This finding of *most* do, *some* don't when it comes to interpretation; and *most* don't, *some* do when it comes to experiencing unjustified psychological outcomes and intention to engage in unwarranted behaviours is comparable to existing empirical studies. However, existing empirical studies discussed in Chapter Four focused their conclusions primarily on the psychological outcomes and behaviours or behavioural intent of the majority – the *most*. This research shifted the focus to the *some*, investigating their psychological outcomes and behavioural intentions from the perspective of actual numbers of individuals affected rather than percentages. When it came to the drug sensitivity test, while *most* would not independently alter their medication regime based on DTCGT results, *some* would, exposing themselves to potential physical harm.

Whenever respondents were offered the opportunity to engage with healthcare, whether for assistance interpreting DTCGT risk results or advice on whether DTCGT drug sensitivity results

warranted changing medication dosages, they took it. This suggests concerns about DTCGT's impact on healthcare systems are bona fide − especially considering the system is not currently prepared. Respondents also indicated intentions to share their genetic information − with family, online, and with companies for use in their research − exposing themselves to potential privacy breaches through re-identification, particularly given that publicly accessible databases of genetic data are increasing in size. Review of analytic detail revealed a range of differences, mostly in terms of intensity of opinion. However, when viewed from the perspective of broad patterns, the most notable finding was the overall similarity in response patterns between Australian and US respondents, suggesting at least a certain amount of 'universality' in how individuals engage with DTCGT results. These results provide a glimmer of hope for those supporting international harmonisation of DTCGT regulation.

While other empirical studies have tended to focus on those who 'matched', concluding there was *no evidence of harm*, it is worth reiterating that this does NOT mean there was *evidence of no harm*. This research, like theirs, found evidence of harm − not for *most* respondents but for *some*. Those who 'mismatched' relative to disease predisposition tests experienced potential consumer detriment through psychological outcomes disproportionate to, and intentions to engage in behaviours not warranted by the actual results presented. And when viewed as actual numbers, not percentages, raise legitimate cause for concern, as these DTCGT consumers were either falsely reassured or unnecessarily worried.

DTCGT's promise of consumer empowerment will only be realised, and those who mismatch exposed to consumer detriment, if individuals purchase tests. Australia's DTCGT industry is currently comparatively small with a few key players, and familiarity and purchase intentions amongst Australian consumers low as evidenced by both this and other Australian research discussed in Chapter Two. However, all available forecasts project significant growth worldwide, with nothing to suggest the Australian market will not also grow, although perhaps not as fast or significantly as some other markets. Whether the proportion of those exposed to consumer detriment will change remains to be seen, however as markets increase, their absolute number will increase concomitantly.

# PART TWO: WHICH DTCGT REGULATORY ROAD TO FOLLOW?

*'We can't uninvent this technology, which may indeed turn out to be a powerful way of helping individuals manage their health better and save health systems billions. But we do need to know how to properly use and regulate it. The time to decide how these things are done has arrived.'*[5]

As lawyers and judges are wont to say, you can't 'unring the bell'.[6] You cannot 'undiscover' genetic advances and 'uninvent' the technology delivering personal genetic information to consumers in their homes, as much is the same science and technology delivering genetic information to patients in their doctors' surgeries. DTCGT is certainly not the only advance in genetic science, technology and translation generating concern and regulatory debate, with the ethical issues surround CRISPR gene editing technology being a case in point.[7] However, DTCGT has been at the forefront of the paradigm shift from medical to consumer, with in-depth analysis of the industry providing insight into how individuals might engage with genetic advances when they are commercialised and removed from the medical sphere. As genetic testing shifts its clinical focus to whole exome and genome sequencing – and whatever comes next – industry will follow once affordable price points can be achieved to make it profitable. The industry will continue to respond to demands from consumers seeking control over their own healthcare and, if more encouragement is needed, companies need only think of the monetary value of the genetic data created by their endeavours.

## *7.2.1 The need for DTCGT regulation*

As noted in Chapters Three and Four, taken collectively, the concerns expressed in the academic commentary, positions statements, and organisational reports suggest the core problem is DTCGT's commercial nature, operating as it does outside traditional healthcare protections. And the consensus is these concerns are sufficiently serious to require regulation.[8]

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[5] Referencing DTCGT. Adrian Burton 'Are we ready for direct-to-consumer genetic testing?' (2015) 14(2) *The Lancet* 138-139.

[6] Expression 'unring the bell' originated in *Sandez, Jr. v. United States of America*, 239 F.2d 239 (9th Cir. 1956).

[7] See Carolyn Brokowski and Mazhar Adli, 'CRISPR Ethics: Moral Considerations for Applications of a Powerful Tool' (2019) 431(1) *Journal of Molecular Biology* 88-101; John Mulvill, Benjamin Capps, Yann Joly, Tamara Lysaght Hub, A. Zwart and Ruth Chadwick, 'Ethical issues of CRISPR technology and gene editing through the lens of solidarity' (2017) 122(1) *BMJ* 17-29.

[8] See Sarah Sunderman, 'The need for regulation of direct-to-consumer genetic testing in the United States: Assessing and applying the German policy model' (2013) 12 *Washington University Global Studies Law Review* 357; Timothy Caulfield, 'Direct-to-consumer testing: if consumers are not anxious, why are policymakers?' (2011) 130 *Hum Genet* 23-25; Jennifer Gniady, 'Regulating Direct-to-Consumer Genetic

From a legal perspective, regulation refers to 'the act or process of controlling or directing by rule, restriction, principle etc.' or, more precisely, 'delegated legislation made pursuant to an Act',[9] with accompanying sanctions for non-compliance. Brownsword and Goodwin define regulation more broadly as 'any instrument (legal or non-legal in its character, government or non-governmental in its source, direct or indirect in its operation, and so on) … designed to channel group behaviour', with persons or bodies initiating this considered 'regulators'.[10]

Regulation can either be principles or rules-based, each with its own advantages and disadvantages. Principles-based regulation provides general rules setting out the overall objectives to be achieved, providing an overarching framework guiding key players that is sufficiently flexible to allow application in new or changing environments − a form of 'future proofing'.[11] However, its general nature and flexibility can result in ambiguity, allowing minimum compliance, avoidance behaviours and inadequate protections. Rules-based regulation, in contrast, is rigid, prescribing detailed steps requiring compliance, aiming to provide high levels of certainty to both regulators and regulatees, but requiring regulators to anticipate future applications. While different in their approach, principles and rules-based regulation can operate as a hybrid system, articulating general principles that can be applied with flexibility to new situations complemented by detailed rules providing clarity − as illustrated by the Australian Consumer Law (ACL) discussed in Chapter Three.

Whichever definition of regulation is applied and whether it is rules or principles-based, DTCGT presents particular challenges to regulators as it not only represents a paradigm shift from medical to consumer, but also is occurring in a rapidly evolving industry space. It has been suggested regulation in a space such as this must be legitimately and ethically appropriate and reflect a consensus of opinion to ensure regulatee acceptance (on both supply and demand sides), while being responsive to technological developments to ensure it is future-proofed − a

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Testing: Protecting the Consumer Without Quashing a Medical Revolution' (2008) 76(5) *Fordham Law Review* 2429-2475.

[9] Ray Finkelstein and David Hammer (eds), *Concise Australian Legal Dictionary* (LexisNexis Butterworths, 5th ed. 2015) 540.

[10] Roger Brownsword and Morag Goodwin, *Law and Technologies of the Twenty-First Century* (Cambridge University Press, 2012) 25.

[11] See Julia Black, *Principles Based Regulation: Risks, Challenges and Opportunities* (2007) London School of Economics and Political Science, <http//:eprints/lse.ac.uk/62814>.

decidedly tall order, especially the latter when considering the rate of change in the genetics sector.[12]

As the majority of DTCGT activity and development continues to be offshore and online, the resulting jurisdictional challenges would also require a level of harmonisation of regulatory approaches on an international level, meaning regulation must accommodate differing belief, legal and healthcare systems.[13] Gaining this level international cooperation in an environment where online jurisdictions are difficult to delineate and any 'globally acting, internet based industry cannot be forced to comply with laws or regulations that are binding only country by country', would be particularly challenging.[14]

To further appreciate the challenges this would involve, consider the current situation in Europe where countries such as France and Germany require genetic testing to be conducted by medical professionals effectively banning DTCGT with potential fines for non-compliance, compared to the UK and Estonia where test kits are sold over-the counter. Countries such as Poland and Romania do not have laws specifically addressing DTCGT, relying on general laws regarding healthcare and patient rights.[15]

### *7.2.2 How DTCGT should be regulated: A grab bag of recommendations*

The commentary concerning why and how DTCGT should be regulated is extensive, approaching the issue from a range of disciplines and perspectives.[16] Some focused on the DTCGT contract. For

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[12] See Roger Brownsword and Morag Goodwin, *Law and the Technologies of the Twenty-first Century* (Cambridge University Press, 2012); Anon, Editorial 'Direct-to-consumer genetic testing' (2012) 380 *The Lancet* 76.

[13] See Amy McGuire, Barbara Evans, Timothy Caulfield and Wylie Burke, 'Regulating direct-to-consumer personal genome testing' (2010) 330 *Science* 181-182.

[14] L Kalokairinou, H Howard, S Slokenberga, E Fisher, M Flatscher-Thöni, M Harlev, R van Hellemondt, J Juškevicius, J Kapelska-Pregowska, P KováL Lovrecic, H Nys, A de Paor, A Phillips, L Pruhill, E Rial-Sebbag, C Casabona, J Sándor, A Schuster, S Soini, K Søvig, D Stoffel, T Titma, T Trokanas and P Borry, 'Legislation of direct-to-consumer genetic testing in Europe: a fragmented regulatory landscape' (2018) 9 *J Community Genet* 117-132, 127. Quoting Christine Hauskeller, 'Direct to consumer genetic testing' (2011) *BMJ* DOI: 10.1136/bmj.d2317.

[15] See Louiza Kalokairinou, H Howard, S Slokenberga, E Fisher, M Flatscher-Thöni, M Harlev, R van Hellemondt, J Juškevicius, J Kapelska-Pregowska, P KováL Lovrecic, H Nys, A de Paor, A Phillips, L Pruhill, E Rial-Sebbag, C Casabona, J Sándor, A Schuster, S Soini, K Søvig, D Stoffel, T Titma, T Trokanas and P Borry, 'Legislation of direct-to-consumer genetic testing in Europe: a fragmented regulatory landscape' (2018) 9 *J Community Genet* 117-132; Rei Fukuda and Fumio Takada, 'Legal regulations on health-related direct-to-consumer genetic testing in 11 countries' (2018) 48 *Kitasato Med* 52-59.

[16] See Gail Javitt, Erica Stanley and Kathy Hudson, 'Direct-to-consumer genetic tests, government oversight, and the First Amendment: What the government can (and can't do) to protect the public's health' (2004) 57(2) *Oklahoma Law* Review 251-302; Jessica Palmer, 'Genetic gatekeepers: Regulating direct-to-consumer

example, Phillips identified potentially unfair contract terms that would likely run foul of existing legislation, while Griggs recommended a 'cooling off' period relative to contract formation.[17]

Other commentators have focused on the DTCGT offering itself. For example, Hauskeller suggested a *voluntary* international quality certificate that 'complies with ethical standards, provisions for counselling, and stringent standards of scientific validity' believing market advantage would encourage compliance.[18] Lippi and colleagues favoured either mandatory applicable ISO accreditation or compliance with OECD genetic testing standards.[19] Skirton, noting the difficulty producing policies acceptable to all stakeholders, suggested codes of practice detailing, for example, the minimum information required by consumers for informed decision-making in consultation with healthcare professionals and tests that should not be offered without included access to genetic counselling from appropriate healthcare professionals.[20] Javitt, Katsanis, Scott and Hudson suggested a mandatory genetic test registry rather than the current voluntary NIH Genetic Testing Registry.[21] Griggs recommended required reading of a mandatory industry-wide statement of the importance of genetic counselling.[22] Some focused specifically on how results were presented, recommending multiple formats and framing risk including graphic representations[23] or recommended presenting only actionable results, although how criteria would be decided was not addressed.[24]

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genomic services in an era of participatory medicine' (2012) 67 *Food and Drug Law Journal* 475-524; Kayte Spector-Bagdady and Elizabeth Pike, 'Consuming Genomics: Regulating direct-to-consumer genetic and genomic information' (2014) 92(4) *Nebraska Law Review* 677-745.

[17] Andelka Phillips, 'Reading the fine print when buying your genetic self online: direct-to-consumer genetic testing terms and conditions' (2017) 36(3) *New Genetics and Society* 273-295; Lynden Griggs, 'Direct-to-consumer genetic testing: The double helix unleashed, problem or panacea?' (2012) 20 *Journal of Law and Medicine* 464-469.

[18] Christine Hauskeller, 'Direct to consumer genetic testing' (2011) *BMJ* DOI: 10.1136/bmj.d2317.

[19] Gail Javitt, Sara Katsanis, Joan Scott and Kathy Hudson, 'Developing the Blueprint for a Genetic Testing Registry' (2010) 13 *Public Health Genomics* 95-105. NIH registry <http://ncbi.nlm.nih.gov/gtr>. Also Guiseppe Lippi, Emmanuel Favaloro and Mario Plebani, 'Direct-to-consumer testing: more risks than opportunities' (2011) 65(12) *International Journal of Clinical Practice* 1121-1229; OECD Guidelines for Quality Assurance in Molecular Genetic Testing 2007 <http://www.oecd.org/science/biotech/38839788.pdf>.

[20] Heather Skirton, Lesley Goldsmith, Leigh Jackson and Anita O'Connor, 'Direct to consumer genetic testing: a systematic review of position statements, policies and recommendations' (2012) 82 *Clin Genet* 210-218.

[21] Gail Javitt, Sara Katsanis, Joan Scott and Kathy Hudson, 'Developing the Blueprint for a Genetic Testing Registry' (2010) 13 *Public Health Genomics* 95-105.

[22] Lynden Griggs, 'Direct-to-consumer genetic testing: The double helix unleashed, problem or panacea?' (2012) 20 *Journal of Law and Medicine* 464-469.

[23] Denise Lautenbach, Kurt Christensen, Jeffrey Sparks and Robert Green, 'Communicating genetic risk information for common disorders in the era of genomic medicine' (2013) 14 *Annu. Rev. Genomics Hum. Genet.* 491=513; J Leighton, K Valverde and B Bernhardt, 'The general public's understanding and perception of direct-to-consumer genetic test results' (2012) 15 *Public Health Genomics* 11-21; Linda

Wright, Hall and Zimmerman suggested five key requirements would adequately protect consumers: consent procedures, formal laboratory accreditation, valid gene-disease evidence, results interpretation by qualified staff, and protection against false or misleading claims.[25] Gniady advocated shoring up existing regulation to ensure quality standards but retaining the existing open market approach.[26] To further complicate the situation, given the bundled nature of DTCGT, McGuire, Evans, Caulfield and Burke noted 'no one regulatory strategy will be suitable for all DTCGT tests'. They suggested a risk-stratified approach with higher regulatory controls placed on higher risk tests.[27]

Empirical research found while most DTCGT consumers expressed the need for a non-governmental (84%) or government (73%) agency to monitor DTCGT claims to ensure consistency with scientific evidence, 66% believed DTCGT should be available without government oversight, suggesting a desire for 'unfettered access to high-quality information'.[28] The vast majority also favoured a policy to ensure law enforcement and insurers would not gain access.

While each of these recommendations has merit, what is notable is the lack of consistent direction to regulators, as each focuses on specific areas, providing limited guidance. For regulation to be effective it must be backed up with effective enforcement, as that is where its real teeth lay, although the deterrent effect of regulation's very existence cannot be denied. Who would be responsible for enforcement depends on each recommendation as they dictate what would be regulated. Which enforcement options are selected depends on what enforcement is intended to achieve – encourage or deter behaviour or punish − with options ranging from

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Cameron, Theresa Marteau, Paul Brown, William Klein and Kerry Sherman, 'Communication strategies for enhancing understanding of the behavioral implications of genetic and biomarker tests for disease risk: The role of coherence' (2012) 35 *J Behav Med* 286-298, 294; Isaac Lipkus, 'Numeric, verbal and visual formats for conveying health risks: suggested best practices and future recommendations' (2007) 27 *Med Decis Making* 696-713.

[24] Tinsley Webster, Sarah Beal and Kyle Brothers, 'Motivation in the age of genomics: why genetic findings of disease susceptibility might not motivate behavior change' (2013) 9(8) *Life Sciences, Society and Policy* <http://www.isspjournal.com/contents/9/1/8>.

[25] Caroline Wright, Alison Hall and Ron Zimmern, 'Regulating direct-to-consumer genetic tests: What is all the fuss about?' (2011) 13(4) *Genetics in Medicine* 295-300.

[26] Jennifer Gniady, 'Regulating direct-to-consumer genetic testing: Protecting the consumer without quashing a medical revolution' (2008) 76 *Fordham Law Review* 2430-2475.

[27] Amy McGuire, Barbara Evans, Timothy Caulfield and Wylie Burke, 'Regulating direct-to-consumer personal genome testing' (2010) 330 *Science* 181-182, 182.

[28] Juli Murphy Bollinger, Robert Green and David Kaufman, 'Attitudes About Regulation Among Direct-to-Consumer Genetic Testing Customers' (2013) 17(5) *Genetic Testing and Molecular Biomarkers* 424-428, 424.

education programs and industry self-regulation through to monetary penalties and criminal charges.[29]

While creating new regulations and regulatory frameworks is possible, the resources needed for enforcement would vary. And enforcement agencies have to have the authority and motivation to enforce. While agencies such as the TGA and ACCC have power to investigate on their own initiative, they would need a reason as enforcement is typically enlivened by adverse incidents or escalating complaints with relevant authorities. Complaints procedures require relatively high levels of consumer knowledge and motivation. Consumers must first recognise there is a cause for complaint which must generate sufficient concern to prompt action, assuming they know which agency and how to lodge their complaint. As noted previously, psychological detriment, essentially *hidden*, is difficult for consumers to recognise.

## PART THREE: NAVIGATING REGULATORY CONGESTION TO PROTECT CONSUMERS

In 2003, when reviewing existing genetics-related regimes, the Australian Law Reform Commission (ALRC) and Australian Health Ethics Committee (AHEC) noted the 'patchwork of federal, state and territory laws; official guidelines; personal and professional ethics; institutional restraints; peer review and pressure; oversight by public funding authorities and professional associations; supervision by public regulatory and complaints-handling authorities; private interest; and market pressure.'[30] This 'patchwork' has become even more complicated with the emergence of DTCGT.[31]

Chapter Three provided an overview of the pathways, processes and protections available in Australia's CGT and DTCGT spaces. What emerged was a complex web of regulatory bodies and regulations that *should* provide adequate protection for individuals in their role as *patient*, or *consumer*, or *research participant*. However, modelling of the DTCGT space revealed individuals do not assume just one role, afforded the protections enlivened by that role. The initial bifurcated pathway to health-related genetic testing − either consumer *or* patient − was shown to have the potential to intersect, either as the result of company-initiated or consumer-initiated engagement

[29] See John Braithwaite, 'The essence of responsive regulation', (2011) 44 *U.B.C. L. Rev.* 475-520.
[30] Australian Law Reform Commission and Australian Health Ethics Committee, *Essentially Yours: The Protection of Human Genetic Information in Australia*, Report No 96 (2003) 34.
[31] See Dianne Nicol and Meredith Hagger, 'Direct-to-consumer genetic testing – a regulatory nightmare?' 198(9) *Medical Journal of Australia* 501-502.

with healthcare. These intersecting pathways resulted in individuals being both *consumer* and *patient*. Allowing DTCGT companies to use personal genetic data in research or voluntarily sharing that data online resulted in individuals being both *consumer* and *research participant*. As such, entering the DTCGT space means individuals could potentially be *consumers* and *patients* and *research participants*.

### *7.3.1 Determining who, what and why*

When addressing whether regulation is required, we first need to determine *who* we are regulating and for *what*; *who* are we trying to protect − consumers, patients *or* research participants − and *what* we are protecting them against. This allows us to then determine *why* new or amended regulation might be required: are existing protections not adequate? This would then allow us to determine *who* should be the regulators and *what* regulation and therefore *what* enforcement efforts would be required.

In the first instance, we might be seeking to regulate medical professionals to ensure those practising have necessary education and experience. Or we might be seeking to regulate businesses to ensure marketplace transactions are fair and the market functions effectively. We might be seeking to regulate those researching on human subject to ensure past abuses of human autonomy can never happen again.

Relative to protection, if trying to protect *consumers*, we would assess the adequacy of protections afforded by the Australian Consumer Law (ACL), those specific to commercial contracts, and ancillary protections such as those offered by the Therapeutic Goods Administration (TGA) relative to in vitro devices (IVDs). If trying to protect *patients*, we would evaluate the Australian Charter of Healthcare Rights, professional and government oversight, and gatekeepers such as Medicare. If trying to protect *research participants* we would assess institutions such as the National Health and Medical Research Council (NHMRC) and international declarations on ethical standards and informed consent.

Determining *what* specifically we are protecting them against allows fine-tuning of the regulatory focus. For example, if concerns relate to DTCGT *marketing* and its commercial *contracts*, we would assess the adequacy of provisions in the ACL, such as those covering misleading and deceptive conduct and unfair contract terms. If the focus is *genetic test validity*, we would assess the 'science' and, for example, standards set by Federal and State authorities for determining which tests are funded. If the focus were the *DNA analysis*, we would assess the standards and

procedures used by laboratories accredited by the National Association of Testing Authorities (NATA).

In reality, with DTCGT, we are trying to protect consumers, patients *and* research participants in *each* distinct aspect of the DTCGT offering and process. At this point, it is worth revisiting Figure 3.12 as it provides an overview of the regulatory space being investigated.

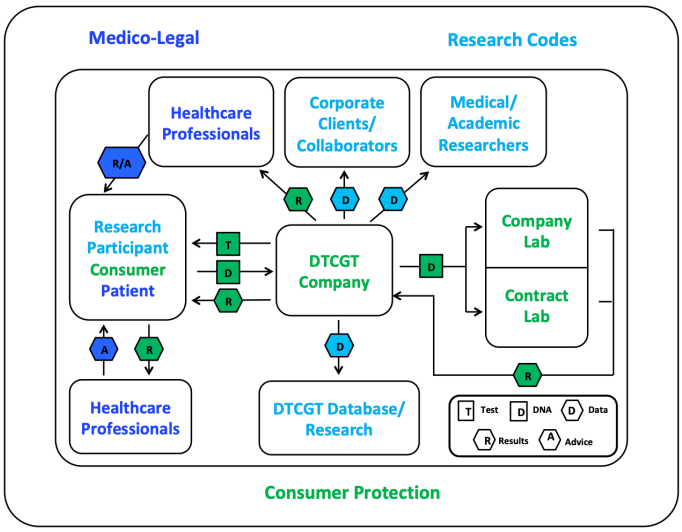


**Figure 7.1 The reality of the DTCGT space**

## *7.3.2 Regulatory silos: Fit for purpose for the old paradigm*

When discussing laws regulating human health research, Laurie noted 'law's tendency to create legal silos of regulatory attention around artificial and fixed objects'.[32] The DTCGT space clearly demonstrates these silos and *who* each seeks to protect and *where*: medical law protects patients in the clinic; consumer protection protects consumers in the marketplace; and research codes protect participants in human health-related research. Regulatory and professional oversight and protections afforded in each of these silos is based on clearly delineated spaces with defined participants and gatekeepers; each with narrowly defined specific expert knowledge, deferring to other experts as required; bound by professional standards, codes of conduct and responsibilities; with delineated authority, responsibility and liability; communicating in each silo's common language through established communication channels; to achieve each silo's overarching and specific objectives. In these silos, *who* is regulated for *what* and *who* needs protecting against *what* is well established and entrenched in bodies of law and established patterns of behaviour.

[32] Graeme Laurie, 'Liminality and the limits of law in health research regulation: What are we missing in the spaces in-between' (2016) 25(1) *Medical Law Review* 47-72, 71.

Determining the adequacy of protections afforded in each of these silos for DTCGT has implications far beyond the DTCGT space. It is reasonable to assume each 'silo' believes it is providing sufficient protection for those within its regulatory ambit, or would be seeking to reform. So, for example, the Australian Charter of Healthcare Rights is assumed to afford sufficient protection for Australian *patients*, regardless of whether GPs are prescribing an antibiotic, surgeons are performing open-heart procedures, or genetic specialists are ordering genetic tests and genetic counsellors providing support. The ACL is assumed to afford adequate protection for Australian *consumers* in *all* commercial transactions, whether the transaction involves a chocolate bar, house mortgage, or DTCGT, ensuring Australia's marketplace operates efficiently and effectively. *Informed consent* is assumed to afford sufficient protection to those participating in health-related research, although the form of that consent remains a hotly debated issue. As such, the regulations created *within* each silo are 'fit for purpose' for each silo.

Regulation in the three distinct spaces however was created under the old paradigm, where these spaces stayed clearly delineated and all parties knew the behaviour expected. When paradigms change, such as the paradigm shift from medical to consumer in the current healthcare space, rigid laws have difficulty adapting − the silos have fortified walls!

Taylor-Alexander and his colleagues suggested 'in circumstances of genuinely disruptive change brought on by rapid advances in technological development, and when this change threatened established behaviours and working practices... regulation can often be called upon to fill new regulatory 'gaps' in a form of rapid response mode … often resulting in ill-conceived and foreshortened regulation that is scarcely fit for purpose.'[33] While referring specifically to human subject health research, they could well have been talking about the 'genetics revolution' generally, or DTCGT specifically, whose disruptive nature was discussed in Chapter Two (2.3.1).

As noted in Chapter Three, when attempting to keep up with advances in the field of genetics, there has been a tendency to 'graft on' new provisions to existing legislation and regulation if possible rather than creating *sui generis* legislation or taking a ‘wait and see’ adverse outcomes approach − the regulatory equivalent of putting it in the 'too hard basket'. 'Grafting on' is generally reactive − with the need usually based on what has already transpired. To be proactive, any new laws or 'grafts' would have to regulate *possibilities* − *possible* negative outcomes that

[33] Samuel Taylor-Alexander, Edward Dove, Isabel Fletcher, Agomoni Ganguli Mitra, Catriona McMillan and Graeme Laurie, ‘Beyond regulatory compression: Confronting the liminal spaces in health research regulation’ (2016) 8(2) *Law, Innovation and Technology* 149-176, 152.

*might* occur if *possible* products or procedures are created, a daunting task in emergent and disruptive sectors such as genetics.

### 7.3.3 Regulatory congestion: Creating regulatory niches and regulatory opportunities

Making recommendations relating to creating new laws or amending existing laws *within* any individual silo would only add additional 'patches' to the 'patchwork' noted by the ALRC and AHEC in 2003. It's not that there is not enough regulation, but rather that there is not the *right* regulation − regulation 'fit for purpose' that adequately protects DTCGT purchasers regardless of their role. The existing patchwork has created significant overlap, with its duplication, inefficiencies and unnecessary burden on regulatees, and perhaps more importantly, gaps − aspects where there is no or limited regulation. For example, DTCGTs not listed on the TGA's register cannot legally be purchased in Australia but can be purchased from offshore companies under exemptions for personal import, a significant gap given DTCGTs essentially online business model.[34]

Overlapping regulatory requirements provide opportunities for businesses to choose to comply with the regulation that is the least onerous, has the least effect on profitability, or is the least likely to be enforced by the regulator, or if they do enforce, has the least penalties. When assessing markets, companies often look for niches − small segments or groups of consumers whose needs are currently unmet or the company believes it can better satisfy. Overlaps, but most particularly gaps, create 'regulatory niches' − which business is good at both finding and exploiting. The commercial imperative driving businesses dictates this is precisely what they *should* and *would* do – in the absence of anything saying they *can't*. As discussed throughout this research, genetic data has significant monetary value, something the DTCGT industry is keen to exploit. Gaps in regulatory schemes provide windows of potentially profitable opportunity.

One case illustrating this relates to online interpretation sites, such as Promethease.[35] These sites allow consumers to upload their personal raw genetic data files provided by DTCGT companies such as 23andMe or DTC companies such as Ancestry.com.[36] For minimal cost, these sites provide

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[34] *Therapeutic Goods (Medical Devices) Regulations 2002* (Cth) Schedule 4 part 1 (1.1) and (1.2).
[35] <https://promethease.com>.
[36] By February 2018, Ancestry.com had accumulated data from over 7 million customers, arguably representing the world's largest genetic database. Antonio Regalado, '2017 was the year consumer DNA testing blew up' 12 February 2018, *Technology Review* <https://www.technologyreview.com/s/610233>.

results for a range of health-related genetic tests, albeit in often difficult to navigate format.[37] These online interpretation sites allow DTCGT consumers to expand their health-related results and DTC consumers to obtain health-related results. While the US Food and Drug Authority (FDA) says it 'has authority to regulate software that interprets genomics', this has not been tested, and whether the TGA would take a similar stand is uncertain.[38] What is certain is direct-to-consumer genetic testing for ancestry, traits and sporting prowess, amongst others, fail to meet the 'therapeutic' bar enlivening TGA authority. Recent research suggests online interpretation sites are proliferating and consumers are increasingly uploading raw genetic data, often to multiple sites.[39] Using multiple sites often generates multiple, potentially conflicting results, echoing results found in the US Government Accountability Office's early investigation of DTCGT discussed in Chapter Four (4.1.1.4).[40]

As with all online commercial sites, interpretation sites are governed by their own Terms of Service and Privacy Policies. For example, before uploading to Promethease, consumers must signify on the site's homepage they understand reports are for 'educational and research purposes only', DNA variations explain only a small part in trait heritability, and should discuss their report with medical professionals, amongst others. The Promethease Privacy Policy, accessible as pop-up, states 'At no time is your DNA data shared – or sold – to any external party, period', although its Terms of Use contains the somewhat ambiguous 'By posting information to this wiki, you grant full publishing and redistribution rights to it.'[41] As online communities such as Patients Like Me have recognised the monetary value in health and genetic data, one has to question how long before this particular 'wiki' changes it terms. Given recent research indicating Promethease was the most frequently used health-related interpretation site, making it '... by

[37] As reported by the consenting individual noted in Chapter Three who purchased two DTCGT tests, the raw data file from one of which was uploaded to Promethease.
[38] Antonio Regalado, 'How a wiki is keeping direct-to-consumer genetics alive' 19 October 2014, *Technology Review* <https://www.technologyreview.com/s/610233>.
[39] Sarah Nelson, 'Consumer genetic testing customers stretch their DNA data further with third-party interpretation websites' *The Conversation* 14 June 2019 <https://theconversation.com/consumer-genetic-testing-customers-stretch-their-dna-data-further-with-third-party-interpretation-websites-118248>. Promethease was the most frequently used health-related online interpretation site. Others include GeneticGenie, Livewello, and Interpretome.
[40] Gregory Kutz, 'Direct-to-consumer genetic tests: misleading test results are further complicated by deceptive marketing and other questionable practices' (2010) <https://www.gao.gov/assets/130/125079.pdf>.
[41] Promethease <https://promethease.com>.

default, the largest purveyors of consumer health genetic services in the United States', the time is likely quickly approaching.[42]

Survey results in Chapter Six clearly showed the *potential* exists for consumer detriment as individuals engage with DTCGT companies and test results. However, whether this potential is judged sufficient or serious enough to warrant policy development and regulatory reform as suggested by the Consumer Policy Toolkit requires further consideration in light of resource implications as well as political and policy priorities. As such, rather than making specific recommendations as to specific changes needed to specific regulations in one or more of the silos, two overarching recommendation are made in this Chapter.

### *7.3.4 What should Australia's regulators do?*

The first recommendation is to *do nothing*.... UNTIL key players from the three identified regulatory spaces are brought together to consider regulating DTCGT from a holistic, sector-wide perspective − in other words, working together to break down the silos, creating regulation that 'fits' the reality of the DTCGT space and adequately protects those purchasing. Whilst doing nothing immediately, the opportunity should be taken to refer this issue to the Australian Law Reform Commission (ALRC). The function of the ALRC is to undertake research and provide recommendations concerning law reform to the Attorney-General of Australia for eventual consideration by the House of Representatives and the Senate.[43] As such, it is well placed to bring the appropriate players from the medico-legal, consumer, and research regulatory spaces together. While this research has focused on DTCGT, the focus of these regulatory reform discussions should not be limited to DTCGT but the coming age of 'personalised medicine' and whatever may follow.

The second recommendation focuses on one of the 'softer' regulatory options − that of genetics education. And genetics education for both the general public and the healthcare sector need not wait until the silos are broken down. Survey results identified the pivotal role played by results interpretation in the affect experienced and behaviours intending to pursue. Respondents who 'mismatched' − interpretation not consistent with actual results − experienced disproportional

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[42] Sarah Nelson, 'Consumer genetic testing customers stretch their DNA data further with third-party interpretation websites' *The Conversation* 14 June 2019 <https://theconversation.com/consumer-genetic-testing-customers-stretch-their-dna-data-further-with-third-party-interpretation-websites-118248>; Antonio Regalado, 'How a wiki is keeping direct-to-consumer genetics alive' 19 October 2014, *Technology Review* <https://www.technologyreview.com/s/610233>.

[43] The ALRC operates under the authority of the *Australian Law Reform Commission Act 1996* (Cth), and the *Public Governance, Performance and Accountability Act 2013* <www.alrc.gov.au>.

affect and intended to engage in behaviours not warranted by DTCGT results – in other words, experienced potential personal non-financial consumer detriment, especially hidden psychological detriment. As individuals self-interpret genetic test results that appear in their inboxes and mailboxes, interpretation does not fit within existing regulations in any of the spheres. Creating new regulations aimed specifically at protecting individuals against 'mismatching', even if proven possible which itself is debatable, would be intrusive and contrary to both the Australian healthcare and legal systems' focus on personal autonomy and the DTCGT sector's promise of consumer empowerment. For example, in medical settings competent individuals over the age of consent can refuse life-saving treatment, while in commercial settings can sign contracts not read, and exchange what they believe to be acceptable consideration.

More effective long term solutions to the interpretation regulatory dilemma lie in educating adults, especially parents, and children about genetics and working to improve health literacy, an admittedly challenging task given the size of the population and its diversity.[44] Such education efforts would not just improve individual engagement with DTCGT but all aspects of 'personalised medicine' – and 'future proof' whatever comes next in both the clinic and marketplace. Specific genetics programs aimed at the healthcare profession need to be fully integrated into initial training and continuing professional development, rather than being offered as 'options'.

## CONCLUDING COMMENTS

Viewed holistically, this research provides a 'glimpse of the future' and insight into individual engagement as genetic discoveries and technological advances will undoubtedly continue to transform healthcare, both in the clinic and the marketplace. DTCGT is simply one disruptive technology, albeit in the vanguard, setting the stage and clearing regulatory hurdles, for those that will undoubtedly follow. During the time this research was conducted, the FDA has banned and subsequently authorised selected 23andMe disease predisposition tests, downclassified all carrier tests, and streamlined regulatory approval processes; whole genome and exome sequencing is reaching increasingly affordable consumer price points; and new genetic associations are being announced daily, with genetic tests rapidly following. And as noted in the 2001 announcement of initial sequencing of the human genome, 'the more we learn about the

[44] See Jane Tiller and Paul Lacaze, 'Regulation of Internet-based Genetic testing: Challenges for Australia and other jurisdictions' (2018) 6(24) *Front. Public Health* DOI:10.3389/pubh.2018.00024; Dianne Nicol, Tania Bubela, Don Chalmers, Jan Charbonneau, et al. 'Precision medicine: drowning in a regulatory soup?' *Journal of Law and the Biosciences*, May 2016, DOI: 10.1093/jlb/lsw018; Dianne Nicol and Meredith Hagger, 'Direct-to-consumer genetic testing – a regulatory nightmare?' (2013) 198(9) *Medical Journal of Australia* 501-502.

human genome, the more there is to explore.'[45] Given this, one cannot but feel a sense of urgency that the 'window of opportunity' for proactive regulatory action is rapidly closing – lest law limp further and further behind.

Whatever the genetics future holds, regulating it will require striking a delicate balance respecting personal autonomy and consumer empowerment while protecting individuals from potential harm and encouraging, rewarding and protecting innovation while avoiding undue strain on overtaxed healthcare systems. This analysis of DTCGT can be used as a lens to view future developments as health, commercial and research spheres will increasingly overlap.

With respect to DTCGT, whether regulators decide to regulate or enforcement agencies enforce, anyone considering purchasing DTCGT should nonetheless be encouraged to *think before you spit ... and share!*

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# Appendices

# APPENDIX ONE: INGREDIENTS FOR MAKING YOU

## *The Book of Life: The total YOU*

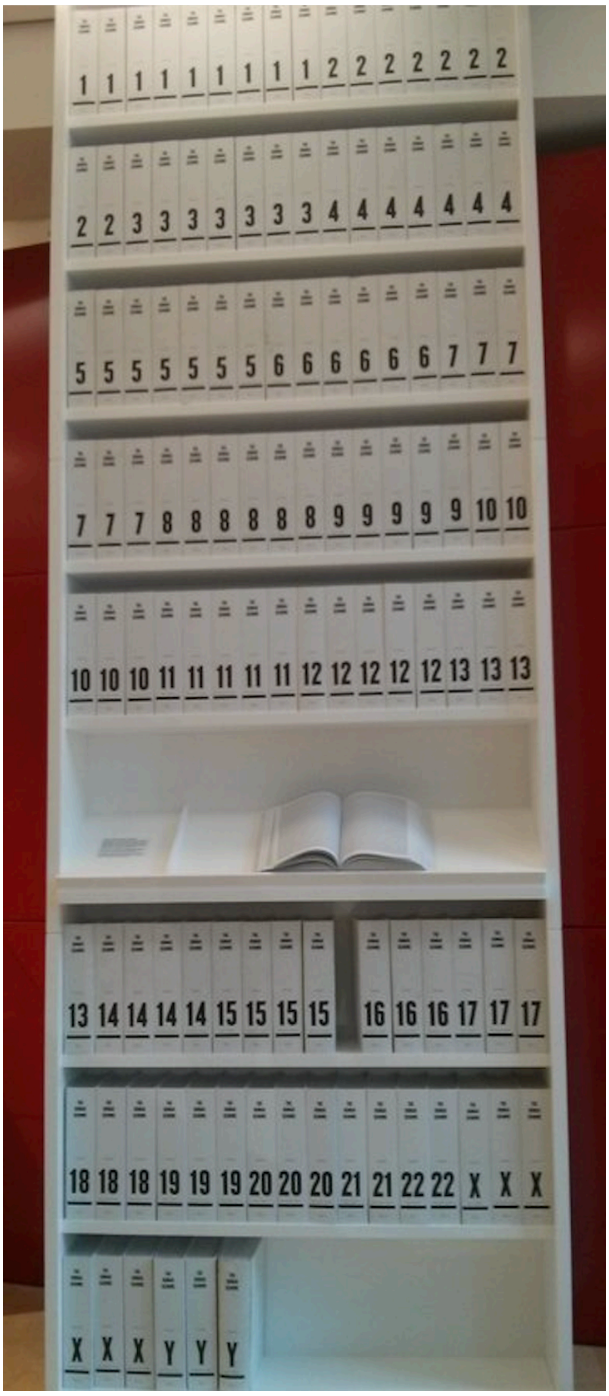



**Figure 1.1.** ***Reference Genome – The Wellcome Trust, London***[1]

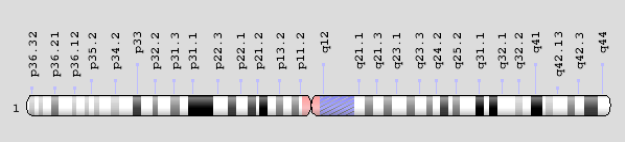
[1] <http://blogs.lshtm.ac.uk/students/2015/03/11/seeing-science-free-london-wellcome-collection/>.

Each page of the reference genome displays the As, Cs, Gs and Ts that collectively are needed to make a human. Autosomal chromosomes are numbered in descending order based on the number of genes on each, followed by the two sex chromosomes. For example, Chromosome 1 is the largest overall containing between 2000 and 2100 genes, with Chromosome 21 the smallest autosomal chromosome with 200 to 300 genes. The Y chromosome is the smallest overall containing just 50 − 60 genes, compared to 800 – 900 genes on the X chromosome.

## *Chromosomes: YOU divided by 23*

Geneticists use idiograms to represent chromosomes' relative size (as illustrated below), with the banding patterns used to describe the precise location of genes. The light and dark bands appear when chromosomes are stained and observed under microscopes. Idiograms indicate the precise location for researchers to use when searching for particular SNPs. (Source: https://ghr.nlm.nih.gov/).

Chromosome 1




X Chromosome

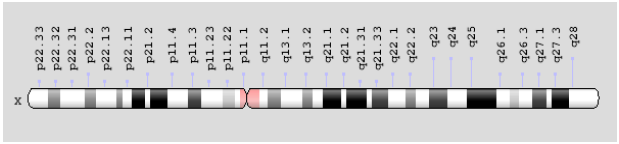



**Figure 1.2. Autosomal & sex chromosomes**

## *Cells: What will this one become?*

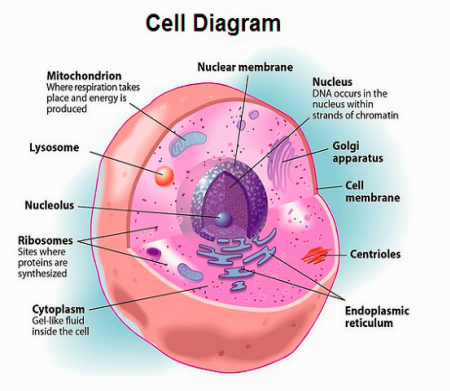



**Figure 1.3.** ***The human cell***[2]

Each cell contains the same core components with cell type dictated by proteins encoded:

- the *nucleus* houses DNA (chromosomes and genes)
- the *nucleolus* makes ribosomal RNA
- the *nuclear membrane* regulates movement of proteins and RNA
- *mitochondria* produces energy
- *lysosomes* break down substances
- *ribosomes* synthesise proteins
- *cytoplasm* is where most chemical processes take place
- *gogli apparatus* secrete and store hormones and enzymes
- *centrioles* help form spindle fibres that separate chromosomes during cell division
- *endoplasmic reticulum* assembles proteins
- the *cell* membrane controls substance movement in and out of cells

[2] <http://getdrawings.com/human-cell-drawing#human-cell-drawing-63.jpg>.

# APPENDIX TWO: ANNOTATED SAMPLE SURVEY

This survey would have been answered by an Australian female allocated into AS(Low) for Type 2 Diabetes, AS(High) for Colorectal Cancer, and Slow metaboliser for drug sensitivity.

The question order, randomisation and questions presented per individual online survey screen are indicated and were the same for all respondents. References for questions adopted or adapted from the literature are included and all questions have been numbered. Details about recoding of variables are also provided.

Questions used to investigate specific concerns as outlined in the literature review are also indicated using the following notations:

**Concerns about the DTCGT offering**

*DTCGT – test quality*
*DTCGT – contract terms*
*DTCGT – purchase likelihood*

**Concerns about the impact on individuals**

*Individual – context*
*Individual – interpretation*
*Individual – affect*
*Individual – behavioural intention*
*Individual – results sharing*

**Concern about the impact on healthcare systems**

*Healthcare*

## Welcome!

You have been invited to participate in a survey being conducted by the University of Tasmania in Australia about direct-to-consumer genetic testing.

The average time for completion of this survey is twenty (20) minutes.

Participation in this survey is completely voluntary.

The information you provide is anonymous and your answers cannot be linked to you personally.

Finally, you may withdraw at any time prior to submitting the results.

Would you like a more detailed explanation of the ethical standards adhered to by this research, or would you like to begin the survey?

- O **Yes please**, I would like more information about the ethical standards of this research.

- O **No thank you**, I am ready to begin this survey.

*This format of selecting whether or not to view the ethics information was allowed as per the Ethics approval.*

If you agree, you will be asked to participate in an online survey that aims to identify understanding of, and reaction to, sample direct-to-consumer genetic test results.

**Additional information about the ethical standards of this research**

Participation in this survey is completely voluntary and you may withdraw at any time prior to submitting the results.

**What happens to this information?**

Only the researchers will have access to the original data, which will be stored on university premises in a locked cupboard for at least five years as prescribed by University of Tasmania regulations.

This study has been approved by the Tasmanian Social Sciences Human Research Ethics Committee. If you have any concerns or complaints about the conduct of this study, please contact the Executive Officer of the HREC (Tasmania) Network on +613 6226 7479 or by email at human.ethics@utas.edu.au. The Executive Officer is the person nominated to receive complaints from research participants. Please quote ethics reference number H0013321.

If you would like to contact the researchers about any aspect of this study, please contact the Chief Investigator:

Professor Dianne Nicol,
Faculty of Law, University of Tasmania
Private Bag 89, Hobart, Tasmania, Australia 7001
Tel: +613 6226 7553
Email: Dianne.Nicol@utas.edu.au

To ensure we get a representative sample, please answer the following questions. Thank you.

*Gender and age were used as qualifiers to ensure sample was broadly representative of these key demographics in both countries. Gender variable used to assign respondents to the appropriate gender-based survey version.*

(1) I am

- **Male**
- **Female**

(2) I am

- **18 – 24 years old**
- **25-44 years old**
- **45-64 years old**
- **Aged 65+**

Age was recoded into *Younger* (18 − 24 + 25 − 44) and *Older* (45 − 64 + 65+).

(3) What is your current **STATE** of residence?

*IP address allowed for initial allocation into appropriate country survey with drop-down menu of appropriate states.*

US states recoded into four census regions used by the U.S. Census Bureau: *South*, *West*, *Northeast* and *Midwest*.

**Welcome to the survey!**

We are interested in what you think about **direct-to-consumer genetic tests**. With direct-to-consumer genetic tests, companies analyse a DNA sample like saliva provided by a consumer and return results directly to the consumer, often online and usually without the involvement of a doctor. Direct-to-consumer genetic tests are for research, information and education only. Test results are not a diagnosis but they can provide information about health conditions that people may have or be at risk of developing in the future.

*This information was provided to ensure all respondents had context for the survey.*

Let's start with a couple of general questions about **direct-to-consumer genetic testing**.

(4) Prior to starting this survey, how familiar were you with direct-to-consumer genetic testing?

| **Not familiar** | **Slightly familiar** | **Somewhat familiar** | **Moderately familiar** | **Extremely familiar** |
|---|---|---|---|---|
| O | O | O | O | O |

Recoded into *Not familiar* (Not familiar), *Somewhat familiar* (Slightly + Somewhat familiar), and *Familiar* (Moderately + Extremely familiar).

(5) What is the likelihood you would purchase a direct-to-consumer genetic test from a company located **INSIDE** your country of residence?

| **Extremely unlikely** | **Unlikely** | **Neutral** | **Likely** | **Extremely likely** |
|---|---|---|---|---|
| O | O | O | O | O |

(6) What is the likelihood you would purchase a direct-to-consumer genetic test from a company located **OUTSIDE** your country of residence?

| **Extremely unlikely** | **Unlikely** | **Neutral** | **Likely** | **Extremely likely** |
|---|---|---|---|---|
| O | O | O | O | O |

*Testing **DTCGT – purchase likelihood.***

Recoded into *unlikely* (extremely unlikely + unlikely), *neutral* (neutral) and *likely* (likely + extremely likely).

We're now going to look at **three** different sets of **direct-to-consumer genetic test results**.

Let's start with our **first** set of **direct-to-consumer genetic test results**. Please read the **first** scenario and answer the questions that follow.

Jennifer has taken a direct-to-consumer genetic test and has just received her Type 2 diabetes test results back online. Jennifer's test results indicate she has a **16.6%** risk of developing Type 2 diabetes over her lifetime. The average person has a **20.7%** risk of developing Type 2 diabetes over their lifetime.

Please indicate your level of agreement with the following statements.

(7) These test results are easy to understand.

| Strongly agree | Agree | Neutral | Disagree | Strongly disagree |
|---|---|---|---|---|
| O | O | O | O | O |

*Testing **Individual – interpretation**.*

Recoded into *Hard to understand* (Strongly + Disagree), *Neutral* (Neutral) and *Easy to understand* (Strongly + Agree).

(8) There is a lot Jennifer can do to prevent developing Type 2 diabetes over her lifetime.

| Strongly agree | Agree | Neutral | Disagree | Strongly disagree |
|---|---|---|---|---|
| O | O | O | O | O |

*Testing **Individual – context**.*

Recoded into *Disagree* (Strongly + Disagree), *Neutral* (Neutral) and *Agree* (Strongly + Agree).

Jennifer has taken a direct-to-consumer genetic test and has just received her Type 2 diabetes test results back online. Jennifer's test results indicate she has a **16.6%** risk of developing Type 2 diabetes over her lifetime. The average person has a **20.7%** risk of developing Type 2 diabetes over their lifetime.

Still thinking about this **first** set of test results, please answer the following:

(9) Based **ONLY** on the test results in this scenario, what is Jennifer's risk of developing Type 2 diabetes over her lifetime?

- Jennifer is **much more likely** to develop Type 2 diabetes than the average person.
- Jennifer is **more likely** to develop Type 2 diabetes than the average person.
- Jennifer has **about the same risk** of developing Type 2 diabetes as the average person.
- Jennifer is **less likely** to develop Type 2 diabetes than the average person.
- Jennifer is **much less likely** to develop Type 2 diabetes than the average person.
- I'm **not sure** what Jennifer's risk is of developing Type 2 diabetes.

*Answer options randomised except for last option. Testing **Individual – interpretation**.*

Recoded into *Low* (much less likely + less likely), *High* (more likely), *Higher* (much more likely), *Same* (about the same risk) and *Not sure* (not sure).

Jennifer has taken a direct-to-consumer genetic test and has just received her Type 2 diabetes test results back online. Jennifer's test results indicate she has a **16.6%** risk of developing Type 2 diabetes over her lifetime. The average person has a **20.7%** risk of developing Type 2 diabetes over their lifetime.

Still thinking about this **first** set of test results, please answer the following:

(10) Imagine that you took a direct-to-consumer genetic test for Type 2 diabetes and your test results were the same as Jennifer's. On a scale of **1 to 5**, please indicate how you would feel.

| | **1** | **2** | **3** | **4** | **5** | |
|---|---|---|---|---|---|---|
| Not worried | O | O | O | O | O | Worried |
| Not anxious | O | O | O | O | O | Anxious |
| Not interested | O | O | O | O | O | Interested |
| Not concerned | O | O | O | O | O | Concerned |
| Not upset | O | O | O | O | O | Upset |
| Not guilty | O | O | O | O | O | Guilty |
| Not relieved | O | O | O | O | O | Relieved |
| Not scared | O | O | O | O | O | Scared |
| Not nervous | O | O | O | O | O | Nervous |
| Not stressed | O | O | O | O | O | Stressed |

*Affect states randomised. Testing **Individual – affect**.*

Reduced into *Emotional distress* and *Engagement.*

Jennifer has taken a direct-to-consumer genetic test and has just received her Type 2 diabetes test results back online. Jennifer's test results indicate she has a **16.6%** risk of developing Type 2 diabetes over her lifetime. The average person has a **20.7%** risk of developing Type 2 diabetes over their lifetime.

(11A) If you took a direct-to-consumer genetic test for Type 2 diabetes and your test results were the same as Jennifer's, how likely is it that you would do **each** of the following?

| | **Extremely unlikely** | **Unlikely** | **Neutral** | **Likely** | **Extremely likely** |
|---|---|---|---|---|---|
| I would go online to find information to help me better understand my genetic test results. | O | O | O | O | O |
| I would feel comfortable sharing my genetic test results with family. | O | O | O | O | O |
| I would not make any decisions based on these test results. | O | O | O | O | O |
| I would go to my doctor to confirm the diagnosis from the direct-to-consumer genetic test. | O | O | O | O | O |
| I would change my diet based on these results. | O | O | O | O | O |
| I would make a special appointment with my doctor to discuss my genetic test results. | O | O | O | O | O |
| I would share my genetic test results in online communities. | O | O | O | O | O |

*Behavioural intention statements randomised within this suite of questions. Testing **Individual – behavioural intention**; **Individual – results sharing**; **Healthcare**.*

*Reduced into Engage with healthcare professionals, Share and seek information, Engage in proactive health behaviours, Take no action and Share with family.*

Jennifer has taken a direct-to-consumer genetic test and has just received her Type 2 diabetes test results back online. Jennifer's test results indicate she has a **16.6%** risk of developing Type 2 diabetes over her lifetime. The average person has a **20.7%** risk of developing Type 2 diabetes over their lifetime.

And finally, still thinking about this **first** set of test results, please answer the following:

(11B) If you took a direct-to-consumer genetic test for Type 2 diabetes and your test results were the same as Jennifer's, how likely is it that you would do **each** of the following?

| | **Extremely unlikely** | **Unlikely** | **Neutral** | **Likely** | **Extremely likely** |
|---|---|---|---|---|---|
| I would monitor my health more closely. | O | O | O | O | O |
| I would not change my exercise habits based on these test results. | O | O | O | O | O |
| I would not feel comfortable sharing my genetic test results with friends. | O | O | O | O | O |
| I would go online to find other people with similar test results. | O | O | O | O | O |
| I would go to my doctor for help in interpreting my genetic test results. | O | O | O | O | O |
| I would go online to get more information instead of visiting my doctor. | O | O | O | O | O |
| I would go to a genetic counsellor to help me better understand my direct-to-consumer genetic test results. | O | O | O | O | O |

*Behavioural intention statements randomised within this suite of questions. Testing* ***Individual – behavioural intention****;* ***Individual – results sharing****;* ***Healthcare****.*

Now we're going to look at our **second** set of **direct-to-consumer genetic test results**. Please read the **second** scenario and answer the questions that follow.

Recoding same as Scenario 1 – Type 2 diabetes

Elizabeth has taken a direct-to-consumer genetic test and has just received her colorectal cancer test results back online. Elizabeth's test results indicate she has a **4.8%** risk of developing colorectal cancer over her lifetime. The average person has a **4.0%** risk of developing colorectal cancer over their lifetime.

Please indicate your level of agreement with the following statements.

(12) These test results are easy to understand.

| Strongly agree | Agree | Neutral | Disagree | Strongly disagree |
|---|---|---|---|---|
| O | O | O | O | O |

*Testing **Individual – interpretation**.*

(13) There is a **NOT** a lot Elizabeth can do to prevent developing colorectal cancer over her lifetime.

| Strongly agree | Agree | Neutral | Disagree | Strongly disagree |
|---|---|---|---|---|
| O | O | O | O | O |

*Testing **Individual – context***.

Elizabeth has taken a direct-to-consumer genetic test and has just received her colorectal cancer test results back online. Elizabeth's test results indicate she has a **4.8%** risk of developing colorectal cancer over her lifetime. The average person has a **4.0%** risk of developing colorectal cancer over their lifetime.

Still thinking about this **second** set of test results, please answer the following:

(14) Based **ONLY** on these test results, what is Elizabeth's risk of developing colorectal cancer over her lifetime?

- Elizabeth is **much more likely** to develop colorectal cancer than the average person.
- Elizabeth is **more likely** to develop colorectal cancer than the average person.
- Elizabeth has **about the same risk** of developing colorectal cancer as the average person.
- Elizabeth is **less likely** to develop colorectal cancer than the average person.
- Elizabeth is **much less likely** to develop colorectal cancer than the average person.
- I'm **not sure** what Elizabeth's risk is of developing colorectal cancer.

*Answer options randomised except for last option. Testing **Individual – interpretation**.*

Elizabeth has taken a direct-to-consumer genetic test and has just received her colorectal cancer test results back online. Elizabeth's test results indicate she has a **4.8%** risk of developing colorectal cancer over her lifetime. The average person has a **4.0%** risk of developing colorectal cancer over their lifetime.

Still thinking about this **second** set of test results, please answer the following:

(15) Imagine that you took a direct-to-consumer genetic test for colorectal cancer and your test results were the same as Elizabeth's. On a scale of **1 to 5**, please indicate how you would feel.

| | **1** | **2** | **3** | **4** | **5** | |
|---|---|---|---|---|---|---|
| Not worried | O | O | O | O | O | Worried |
| Not anxious | O | O | O | O | O | Anxious |
| Not interested | O | O | O | O | O | Interested |
| Not concerned | O | O | O | O | O | Concerned |
| Not upset | O | O | O | O | O | Upset |
| Not guilty | O | O | O | O | O | Guilty |
| Not relieved | O | O | O | O | O | Relieved |
| Not scared | O | O | O | O | O | Scared |
| Not nervous | O | O | O | O | O | Nervous |
| Not stressed | O | O | O | O | O | Stressed |

*Affect states randomised. Testing **Individual – affect**.*

Elizabeth has taken a direct-to-consumer genetic test and has just received her colorectal cancer test results back online. Elizabeth's test results indicate she has a **4.8%** risk of developing colorectal cancer over her lifetime. The average person has a **4.0%** risk of developing colorectal cancer over their lifetime.

(16A) If you took a direct-to-consumer genetic test for colorectal cancer and your test results were the same as Elizabeth's, how likely is it that you would do **each** of the following?

| | **Extremely unlikely** | **Unlikely** | **Neutral** | **Likely** | **Extremely likely** |
|---|---|---|---|---|---|
| I would monitor my health more closely. | O | O | O | O | O |
| I would not change my exercise habits based on these test results. | O | O | O | O | O |
| I would not feel comfortable sharing my genetic test results with friends. | O | O | O | O | O |
| I would go online to find other people with similar test results. | O | O | O | O | O |
| I would go to my doctor for help in interpreting my genetic test results. | O | O | O | O | O |
| I would go online to get more information instead of visiting my doctor. | O | O | O | O | O |
| I would go to a genetic counsellor to help me better understand my direct-to-consumer genetic test results. | O | O | O | O | O |

*Behavioural intention statements randomised within this suite of questions with the two suites of questions reversed from Scenario 1. Testing* ***Individual – behavioural intention***; ***Individual – results sharing***; ***Healthcare****.*

Elizabeth has taken a direct-to-consumer genetic test and has just received her colorectal cancer test results back online. Elizabeth's test results indicate she has a **4.8%** risk of developing colorectal cancer over her lifetime. The average person has a **4.0%** risk of developing colorectal cancer over their lifetime.

(16B) And finally, still thinking about this **second** set of test results, please answer the following:

If you took a direct-to-consumer genetic test for colorectal cancer and your test results were the same as Elizabeth's, how likely is it that you would do each of the following?

| | **Extremely unlikely** | **Unlikely** | **Neutral** | **Likely** | **Extremely likely** |
|---|---|---|---|---|---|
| I would go online to find information to help me better understand my genetic test results. | O | O | O | O | O |
| I would feel comfortable sharing my genetic test results with family. | O | O | O | O | O |
| I would not make any decisions based on these test results. | O | O | O | O | O |
| I would go to my doctor to confirm the diagnosis from the direct-to-consumer genetic test. | O | O | O | O | O |
| I would change my diet based on these results. | O | O | O | O | O |
| I would make a special appointment with my doctor to discuss my genetic test results. | O | O | O | O | O |
| I would share my genetic test results in online communities. | O | O | O | O | O |

*Behavioural intention statements randomised within this suite of questions with the two suites of questions reversed from Scenario 1. Testing **Individual – behavioural intention**; **Individual – results sharing**; **Healthcare**.*

We're now going to look at our **third** and **final** set of **direct-to-consumer genetic test results**. Please read the **third** scenario and answer the following questions.

Brenda currently takes **2 pills twice a day** of blood-thinning drugs prescribed by her doctor. Brenda has taken a direct-to-consumer genetic test and has just received her drug response results back online. Brenda's test results indicate she is a **slow** metaboliser of these blood-thinning drugs compared to the average person.

(17) Please indicate your level of agreement with the following statements.

These test results are easy to understand.

| Strongly agree | Agree | Neutral | Disagree | Strongly disagree |
|---|---|---|---|---|
| O | O | O | O | O |

*Testing **Individual – interpretation**.*

Recoding same as Scenario 1.

(18) If my test results for drug responses were the same as Brenda's, I would not make any decisions based on them.

| Strongly agree | Agree | Neutral | Disagree | Strongly disagree |
|---|---|---|---|---|
| O | O | O | O | O |

*Testing **Individual – behavioural intention**.*

Recoded into *Disagree* (Strongly + Disagree), *Neutral* (Neutral) and *Agree* (Strongly + Agree).

Brenda currently takes **2 pills twice a day** of blood-thinning drugs prescribed by her doctor. Brenda has taken a direct-to-consumer genetic test and has just received her drug response results back online. Brenda's test results indicate she is a **slow** metaboliser of these blood-thinning drugs compared to the average person.

(19) Imagine that you took a direct-to-consumer genetic test for drug responses and your test results were the same as Brenda's. On a scale of **1 to 5**, please indicate how you would feel.

| | **1** | **2** | **3** | **4** | **5** | |
|---|---|---|---|---|---|---|
| Not worried | O | O | O | O | O | Worried |
| Not anxious | O | O | O | O | O | Anxious |
| Not interested | O | O | O | O | O | Interested |
| Not concerned | O | O | O | O | O | Concerned |
| Not upset | O | O | O | O | O | Upset |
| Not guilty | O | O | O | O | O | Guilty |
| Not relieved | O | O | O | O | O | Relieved |
| Not scared | O | O | O | O | O | Scared |
| Not nervous | O | O | O | O | O | Nervous |
| Not stressed | O | O | O | O | O | Stressed |

*Affect states randomised. Testing **Individual – affect**.*

Reduced into *Emotional distress* and *Engagement*.

Brenda currently takes **2 pills twice a day** of blood-thinning drugs prescribed by her doctor. Brenda has taken a direct-to-consumer genetic test and has just received her drug response results back online. Brenda's test results indicate she is a **slow** metaboliser of these blood-thinning drugs compared to the average person.

(20) And finally, still thinking about this **third** set of test results, please answer the following question.

If I took a direct-to-consumer genetic test for drug responses and my test results were the same as Brenda's,

- I would **increase** the total number of blood-thinning pills I take daily.
- I would **decrease** the total number of blood-thinning pills I take daily.
- I would **not change** the total number of blood-thinning pills I take daily.
- I would **only change** the total number of blood-thinning pills I take daily after I had discussed it with my doctor.

*Behavioural intention statements randomised. Testing* ***Individual – behavioural intention****;* ***Healthcare****.*

Recoded into *Alter* (increase + decrease), *Not change* (not change) and *Consult doctor* (only change).

Some final questions about direct-to-consumer genetic testing.

(21) Please indicate how much you agree with the following statements.

| | **Strongly agree** | **Agree** | **Neutral** | **Disagree** | **Strongly disagree** |
|---|---|---|---|---|---|
| I am confident the results of direct-to-consumer genetic tests provide all of the information I need to make informed healthcare decisions. | O | O | O | O | O |
| I would be happy for the direct-to-consumer genetic testing company to make my genetic test information available at no cost to researchers in colleges or universities. | O | O | O | O | O |
| I am confident in my ability to interpret genetic test results. | O | O | O | O | O |
| I am confident my personal genetic information will only be shared with other people with my permission. | O | O | O | O | O |
| I would be happy for the direct-to-consumer genetic testing company to use my genetic test information for their research even if I get no financial or other benefit. | O | O | O | O | O |
| I am confident the results of direct-to-consumer genetic tests are accurate. | O | O | O | O | O |
| I would be happy for my genetic test information to be sold for profit by the direct-to-consumer genetic testing company to another company for their research. | O | O | O | O | O |

*Statements randomised. Testing* ***DTCGT – test quality***; ***DTCGT – contract terms***; ***Individual – context***; ***Individual – results sharing***.

Confidence recoded into *Not confident* (Strongly + Disagree), *Neutral* (Neutral) and *Confident* (Strongly + Agree).

DTCGT research recoded into *Unwilling* (Strongly + Disagree), *Neutral* (Neutral) and *Willing* (Strongly + Agree).

(22) What is the likelihood you would purchase a direct-to-consumer genetic test if you provided your DNA sample to the company but the company returned your test results to your doctor?

| **Extremely unlikely** | **Unlikely** | **Neutral** | **Likely** | **Extremely likely** |
|---|---|---|---|---|
| O | O | O | O | O |

*Testing **DTCGT – purchase likelihood**.*

(23) Have you ever purchased a direct-to-consumer genetic test?

| | **Yes** | **No** |
|---|---|---|
| For yourself | O | O |
| For someone else | O | O |

*Testing **DTCGT – purchase likelihood**.*

Recoded into *Purchased* (yes for either) and *Not purchased* (no for both). While asked about DTC tests in general, even if not DTCGT, respondents purchasing would be familiar with the process of providing DNA samples and self-interpreting results.

Now some general questions about health and sources of health-related information.

(24) Which of the following represents the biggest risk of getting a disease?

| **1 in 100** | **1 in 1000** | **1 in 10** |
|---|---|---|
| ○ | ○ | ○ |

*Answer options randomised. Testing **Individual – context**.*

Recoded into *correct* (1 in 10) and *incorrect* (1 in 100 + 1 in 1000).

From Isaac Lipkus, Greg Samsa and Barbara Rimer, 'General Performance on a Numeracy Scale among Highly Educated Samples' (2001) 21(37) *Medical Decision Making* 37-44, 40. Also used in HINTS surveys (<http://hints.cancer.gov>),and academic research such as Samuel Smith, Lindsay Kobayashi, Michael Wolf, Rosalind Raine, Jane Wardle and Christian von Wagner, 'The associations between objective numeracy and colorectal cancer screening knowledge, attitudes and defensive processing in a deprived community sample' (2014) 21(8) *Journal of Health Psychology* 1-11.

(25) A doctor has told a patient to take 2 pills, 4 times a day. How many pills should the patient take in 3 days? Please type your answer **in number form** in the space below.

*Testing **Individual – context***. Recoded into *correct* (24) and *incorrect* (all other answers).

From the *Numeracy Initial Assessment User Workbook*, January 2010, used by the UK's Skills for Health to assess patient numeracy and ability to self-manage healthcare <http://www.skillsforhealth.org.uk>. 'Tablet' changed to 'pill' as more commonly used in AU and US.

(26) Please indicate how much you agree or disagree with the following statements.

| | Strongly agree | Agree | Neutral | Disagree | Strongly disagree |
|---|---|---|---|---|---|
| I'm alert to changes in my health.[1] | O | O | O | O | O |
| Lifestyle is not at all important in determining whether someone develops colorectal cancer. | O | O | O | O | O |
| My health depends on how well I take care of myself.[2] | O | O | O | O | O |
| Family history is not at all important in determining whether someone develops diabetes. | O | O | O | O | O |
| I only worry about my health when I get sick.[3] | O | O | O | O | O |
| Family history is very important in determining whether someone develops colorectal cancer. | O | O | O | O | O |
| There is little I can do to prevent illness.[4] | O | O | O | O | O |
| I have control over whether I will develop a disease even if I am at increased genetic risk.[5] | O | O | O | O | O |
| Lifestyle is very important in determining whether someone develops diabetes. | O | O | O | O | O |
| If genetics causes a disease there is nothing that I can do to reduce the risk of getting the disease.[6] | O | O | O | O | O |
| I take responsibility for the state of my health.[7] | O | O | O | O | O |

*Statements randomised. Testing **Individual – context**.*

Reduced into *health active* and *health passive*.

[1] From Stephen Gould, 'Consumer attitudes towards health and health care: A differentiation perspective' (1990) 22(1) *Journal of Consumer Affairs* 96 − 118, 102; and Nina Michaelidou and Louise Hassan, 'The role of health consciousness, food safety concern and ethical identity on attitudes and intentions towards organic food' (2008) 32(1) *International Journal of Consumer Studies* 163 − 170.

[2] From Mohan Dutta-Bergman, 'Primary Sources of Health Information: Comparisons in the Domain of Health Attitudes, Health Cognitions and Health Behaviours' (2004) 16(3) 273 − 288, 281.

[3] From Frederic Kraft and Philips Goodell, 'Identifying the health conscious consumer' (1993) 13(3) *Journal of Health Care Marketing* 18 − 25, 23.

[4] From Christine Moorman and Erika Matulich, 'A Model of Consumers' Preventive Health Behaviors: The role of Health Motivation and Health Ability' (1993) 20(2) *Journal of Consumer Research* 208 − 228.

[5 6] Based on measures from Lijiang Shen, Celeste Condit and Lanelle Wright, 'The Psychometric Property and Validation of a Fatalism Scale' (2009) 24(5) *Psych Health* 597 − 613.

[7] From Nina Michaelidou and Louise Hassan, 'The role of health consciousness, food safety concern and ethical identity on attitudes and intentions towards organic food' (2008) 32(1) *International Journal of Consumer Studies* 163 − 170, 170.

(27) Thinking about the **last 12 months**, please indicate how often you have engaged in the following activities.

| | Never | Occasionally | Regularly |
|---|---|---|---|
| Looked for health information on the Internet | O | O | O |
| Talked to your family about health issues | O | O | O |
| Used information from the Internet to make a self-diagnosis | O | O | O |
| Shared health-related information in online communities | O | O | O |
| Shared genetic information in online communities | O | O | O |

*Activities randomised. Testing – **Individual – context**.*

(28) Please indicate how much do you trust the following sources of health-related information?

| | A lot | Some | A little | None |
|---|---|---|---|---|
| Doctors | O | O | O | O |
| Family | O | O | O | O |
| Friends | O | O | O | O |
| The Internet | O | O | O | O |
| Health-related online communities | O | O | O | O |

*Sources randomised. Testing – **Individual – context**.*

Question and scale based on HINTS survey question 'In general, how much would you trust information about health or medical information from ...?' with 'health-related online communities' added.

And finally, some questions about **YOU**. Please be assured that **ALL** of your responses remain **STRICTLY CONFIDENTIAL.**

(29) In general, compared to other people my age, my health is:

| **Very good** | **Above average** | **Average** | **Below average** | **Very poor** |
|---|---|---|---|---|
| O | O | O | O | O |

Recoded into *below average* (very poor + below average), *average* (average), and *above average* (above average + very good).

From Bupa online health assessment tool <https://www.oha.bupa.com.au>. Bupa is a major international health insurer and provider of health and well-being resources.

(30) On a scale of **1 to 5**, how would you describe your regular diet?

| | **1** | **2** | **3** | **4** | **5** | |
|---|---|---|---|---|---|---|
| Very healthy | O | O | O | O | O | Very unhealthy |

(31) Thinking about an average week, on how many days would you typically exercise for at least 20 minutes?

| **7 days** | **6 days** | **5 days** | **4 days** | **3 days** | **2 days** | **1 day** | **0 days** |
|---|---|---|---|---|---|---|---|
| O | O | O | O | O | O | O | O |

Diet and exercise answers were combined and recoded into *unhealthy* (combined scores of 1, 2, 3, 4 & 5), *moderately healthy* (combined scores of 6 & 7) and *healthy* (combined scores of 8, 9, 10, 11 & 12).

(32) Do you have a family history of:

| | **Yes** | **No** | **Not sure** | **Prefer not to answer** |
|---|---|---|---|---|
| Diabetes | O | O | O | O |
| Colorectal Cancer | O | O | O | O |

(33) Do you currently take any drugs that are prescribed by a doctor?

- O **Yes**
- O **No**
- O **Prefer not to answer**

(34) In what year were you born?

*A drop-down menu listed years from 1930 to 1997.*

(35) Which of the following **BEST** describes your marital status?

| Married | Living as married | Separated or divorced | Widowed | Never married |
|---|---|---|---|---|
| O | O | O | O | O |

Recoded into *married* (married + living as married) and *not married* (separated or divorced + widowed + never married).

(36) Including yourself, how many people are there in your household?

*A drop-down menu listed the following: 1, 2, 3 – 5, 6 – 8, 9 – 12, 12+.*

** This question was not used in analysis in favour of marital status and children.

(37) How many children under the age of 18 are in your household?

*A drop-down menu listed the following: 0, 1, 2, 3 – 6, 7 – 9, 10+.*

Children was recoded into *Yes* (1 – 10+ children) and *No* (0).

(38) What is the **HIGHEST** level of education you have completed?

- O Some high school / secondary school
- O High school graduate / Year 12 graduate
- O Some college/ university
- O College / university diploma or degree
- O Graduate / postgraduate degree

Recoded into *secondary school* (some high school/secondary school + high school/Year 12 graduate), *college/university* (some college/university + college/university diploma or degree) and *postgraduate* (graduate/postgraduate degree).

39) When asked your ethnic identity, what do you usually say? Please type your answer in the space below.

- Prefer not to answer

** The ethnic identity question confirmed the majority of respondents in both countries identified as Caucasian or Australian/American. While ethnic identity is not considered further, these results should be kept in mind as no claims can be made as to ethnic diversity.

(40) Which of the following **BEST** describes your current work status?

- Employed full time
- Employed part time
- Self-employed
- Home duties
- Student
- Retired
- Unemployed

*Employment status options randomised.*

Recoded into *paid* (employed full time + employed part time + self-employed), *not paid* (home duties + retired + unemployed) and *student* (student).

(41) Which of the following **BEST** describes your combined annual household income?

- Under $25,000
- $25,000 – $34,999
- $35,000 – $49,999
- $50,000 – $74,999
- $75,000 – $99,999
- $100,000 – $149,999
- $150,000 – $199,999
- $200,000 and over
- Prefer not to answer

*Testing **Individual – context**.*
Recoded into *under $50,000* (under $25,000 + $25,000 – $34,999 +$35,000 – $49,999), *under $150,000* ($50,000 – $74,999 + $75,000 – $99,999 + $100,000 – $149,999), *over $150,000* ($150,000 – $199,000 + $200,000 and over) and *Refused*.

**THANK YOU SO MUCH FOR COMPLETING THIS SURVEY. YOUR INPUT IS GREATLY APPRECIATED!**

UNIVERSITY *of* TASMANIA

AUSTRALIA

# APPENDIX THREE: STATISTICAL TESTS CONDUCTED

This appendix explains the statistical tests that were conducted and provides an indication as to the questions each test was used to answer.[3]

## *3.1 Testing for associations: Chi-square analysis*

Chi-square analysis determines if respondent answers for one variable differ based on their responses for another variable. Chi-square tests measure how well observed distributions of variables 'fit' with distributions expected if variables were independent (or occurred by chance). This analysis generates frequencies (%), p values, adjusted residuals and effect sizes.

Cross tabulations produce frequencies indicating percentages of respondents who selected each specific answer option in variable one in combination with each specific answer option in variable two. The Pearson correlation co-efficient, commonly called the p value, determines if the frequencies (%) of both variables are statistically associated.

Statistical significance is the probability observed differences between two variables is due to chance. P values range from 0 to +1 indicating positive and negative associations, with a value of 0 indicating no association. With positive associations, as the value of one variable increases, so too does the value of the other variable. A negative association indicates an inverse relationship. A p value < 0.05 indicates there is a more than 95% chance that the value of the Chi-square (or other statistic) is not random (confidence level of 95%: 5% chance association is random) while a p value < 0.001 indicate 99.99% chance the statistical results is not random (0.01% chance association is random). P values are used to determine statistical significance in a range of different tests.

Adjusted residuals identify specifically where statistically significant differences occur, indicating direction (positive or negative) and quantum of the difference between observed values (actual relationship) and expected values (random relationship). Adjusted residuals above or below 1.97 (rounded to +/- 2.00) indicate statistical significance at $p < 0.05$ while those above or below 3.29 (rounded to +/- 3.30) are significant at $p < 0.001$.

While p values indicate statistical significance, effect sizes provide quantitative measures of strength or degree to which two variables are associated overall. With large samples, statistical

[3] See Michael Finkelstein and Bruce Levin, *Statistics for Lawyers* 3e (Springer, 2015); Julie Pallant, *SPSS Survival Manual* 6e (Allen & Unwin, 2016).

tests generally demonstrate a significant difference, unless there is no effect at all. However, 'very small differences, even if significant, are often meaningless'.[4] Cohen and Glass suggest the product of research inquiries should be effect sizes, not P values allowing researchers to not just identify an effect, but assess its magnitude.[5]

Effect size is used as a post-test to determine strength of association after chi-square analysis has determined statistical significance. The specific post-test used depends on the number of values (answer options) per variable. Phi is used for 2x2 data tables where each variable has two answer options while Cramer's V is used for all others.[6] For this research, effect sizes were categorised as weak (.10 to .29), moderate or strong and interpreted using Cohen's categorisation.[7] Effect sizes were rounded from .295 to .30 for moderate effects and from .495 to .50 for large effects. Effects between .280 and .294 were noted as small verging on moderate and .480 to .494 as moderate verging on large.[8] Taken together, this analysis identifies if relationships between two variables are significant (p value), where differences occur (% and adjusted residuals), and the overall strength (effect size).

Chi-squares were conducted on all variables, seeking to answer questions such as: Are AU respondents more likely than US respondents to search online for health information?

## *3.2 Reducing data: Exploratory and Confirmatory factor analysis*

A composite measure refers to the reduction of a number of measures or scores into one overall total or composite score – a combined dependent variable. When attempting to measure a complex or unobservable construct (e.g. psychological outcomes *cf.* a person's height), it is typical to use a number of questions that are designed to measure the same thing. These measures are often referred to as 'indicators' as they are theoretically expected to measure an indicator of a construct rather than measure it directly. Once measured, statistical tests can determine if the indicators are all associated, as would be expected if they were all measuring the same construct. If this is the case, an underlying construct is present influencing the scores on all of the indicators.

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[4] Gail Sullivan and Richard Feinn 'Using effect size – or why the *P* value is not enough' (2012) September *Journal of Graduate Medical Education* 279-282, 280.
[5] Ibid 279, quoting Cohen and Glass.
[6] See Harald Cramér, *Mathematical Methods of Statistics* (Princeton University Press, 1946).
[7] See Jacob Cohen, *Statistical power analysis for the behavioural sciences* (Lawrence Erlbaum Associates, 2nd ed, 1988), 79-81.
[8] See Christopher Ferguson, 'An effect size primer: A guide for clinicians and researchers' (2009) 40(5) *Professional Psychology: Research and Practice* 532-538; Joseph Durlak, 'How to select, calculate and interpret effect sizes' (2009) 34(9) *Journal of Pediatric Psychology* 917-928.

One single composite score is created and assumed to measure the construct in all subsequent analysis.

Exploratory and Confirmatory factor analyses are data reduction techniques used to identify latent or underlying patterns of correlation, allowing creation of composite measures. Both techniques identify relationships between observed measures (respondent answers) and latent or underlying variables (called factors) accounting for variation and covariation in these measures. Exploratory factor analysis (EFA) is generally used early to explore whether an underlying structure to a relatively large set of variables is suggested.[9] Confirmatory factor analysis (CFA) is used later to confirm specific hypotheses tested or theories concerning the underlying structure identified in EFA or existing theories or models.[10]

CFA is a form of structured equation modelling looking at relationships between observed measures (e.g. respondent answers to specific questions) and latent variables, in addition to identifying the number and nature of any factors. CFA also allows for comparison of alternative models and the structure of models across independent groups e.g. countries.

EFA and CFA were conducted to create composite measures, seeking to answer questions such as: Is there an underlying structure to the ten different affect variables tested to assess psychological outcomes in response to DTCGT test results?

## 3.3 *Testing for differences: T-tests, ANOVAs, Repeated Measures ANOVAs and MANOVAs*

Where appropriate, means and standard deviations were calculated. The mean is the mathematical average of all continuous variables, calculated by summing all scores and then dividing by the number of scores. The standard deviation (SD) indicates how much individual scores deviate from the mean with a high SD indicating a large spread and a low SD indicating a narrow spread. When interpreting means, the scale used must always be considered. For example, a mean of 4 on a 5-point scale would be considered high while a mean of 2 would be considered low. However, if a 3-point scale was used, then a mean of 2 would be considered on the higher end and interpreted accordingly.

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[9] See Leandre Fabigar, Duane Wegener, Robert MacCallum and Erin Strahan, 'Evaluating the use of exploratory factor analysis in psychological research' (1999) 4(3) *Psychological Methods* 272-299, 272.
[10] See Karl Gustav Jöreskog, 'A general approach to confirmatory maximum likelihood factor analysis' (1969) 34(2) *Psychometrika* 183-202.

T-tests, One-way ANOVAs (Analysis of Variance), Repeated Measures ANOVAs and MANOVAs (Multivariate Analysis of Variance) allow comparison of mean scores to determine if observed group differences are statistically significant. These tests are parametric tests where assumptions are made about the parameters of the population tested. These tests all assume the dependent variable fits a normal distribution around the central value with no bias left or right. With a normal distribution, 68% of the respondents fall within +/- 1 standard deviation of the mean, 95% within +/- 2 and 99.7% within +/- 3. Means are compared by deeming one variable as the independent variable (IV), determining if that variable generates statistically significant differences in a continuous variable (dependent variable or DV).

Statistical significance allows rejection of the null hypothesis – that the IV exerts no influence on the DV indicating there is no relationship between variables tested. Interpretation of the statistical significance allows determination of the strength of the alternative hypothesis – that the IV exerts influence on the DV indicating there is a relationship between variables tested.

### *T-tests*

T-tests compare means when the deemed IV has two answer options or levels, for example male compared to female. Independent sample t-tests were conducted as data was collected on a continuous variable (DV) but from two different groups (respondents in Australia or the US).

T-tests were conducted to answer questions such as: Do AU respondents express higher or lower mean likelihood to purchase from an onshore company compared to US respondents? (IV = country; DV = purchase likelihood)

### *ANOVAs*

ANOVAs compare means when deemed independent variables have three or more answer options e.g. Yes, No and Unsure. ANOVAs analyse the variation in means both within and across groups to determine the impact of the IV on the DV. ANOVAs compare the variance in scores between different groups (assumed due to IV) with the variability within each group (assumed due to chance). One-way ANOVAs where there is only one DV were conducted as the impact of only one IV was tested.

While ANOVAs indicate whether groups are significantly different, post hoc tests determine which specific pairs of means are significantly different from each other. There are a range of different post-hoc tests available however the majority operate in the same manner, comparing all pairs of

means (called pairwise comparisons).[11] In this research, post hoc tests using Student-Newman-Keuls (SNK) were conducted. Student-Newman-Keuls uses a stepwise multiple comparison procedure to identify sample means that are significantly different from each other. This test was selected as it maximises statistical power and is appropriate when exploring differences where effect sizes are not known (e.g. new research). As statistically significant differences may be due to the high level of statistical power, a conservative approach to interpretation was taken.

ANOVAs were conducted to answer questions such as: Does overall confidence in DTC tests influence mean likelihood of purchase from an offshore company? (IV = overall confidence; DV = purchase likelihood)

### *Repeated measures ANOVA*

Repeated measures ANOVA (RMA) compare the mean scores of the same respondents on three or more related questions measured on the same continuous or deemed continuous scale. RMAs determine if differences in each question's mean scores are statistically significant from each other (p value). One-way repeated measures ANOVA were conducted as only one IV was tested. RMAs also confirmed whether respondents independently evaluated each individual question, acting as a quality control measure.

Repeated measures ANOVAs were conducted to answer questions such as: Does mean respondent understanding differ based on the type of DTCGT test? (IV = test type, DV = understanding)

### *MANOVAs*

Multivariate analysis of variance (MANOVA) analyses variance in means, comparing groups on more than one dependent variable.[12] The DVs must either be directly or conceptually related e.g. measuring the same or similar construct. The factors identified in the Exploratory and Confirmatory factor analysis for the Psychological outcomes were used in the MANOVA analysis as they were associated as would be expected.

MANOVAs compare groups to determine whether mean differences of groups on the combined DVs are statistically significant. MANOVAs also provide univariate (individual) results for each DV,

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[11] See Hae-Young Kim 'Statistical notes for clinical researchers: *post-hoc* multiple comparisons' (2015) *Restorative Dentistry & Endodontics* 172-176.

[12] MANOVAs are one of the most common multivariate statistical methods in psychological research. See Russell Warne 'A Primer on Multivariate Analysis of Variance (MANOVA) for Behavioural Scientists', Practical Assessment, Research & Evaluation, 19(7), November 2014, http://pareonline.net/getvn.asp?v=19&n=17.

essentially a separate ANOVA for each DV. The same analysis could be conducted using ANOVAs for each DV however the more analyses run, the greater the likelihood of Type I errors. MANOVAs adjust for this increased risk of Type 1 errors. A Type I error is the rejection of a true null hypothesis or a 'false positive': finding significance when there really is none (always a possibility with large sample sizes). A Type II error is retaining a false null hypothesis or a 'false negative': finding no significance where there are actually significant differences between groups.

MANOVAs were conducted (95% confidence level) for the two disease predisposition tests to answer questions such as: Does the *emotional distress* experienced differ based on the Actual severity level respondents were randomly allocated for the sample Type 2 Diabetes test results? (IV = actual severity random allocation; DV = *emotional distress*)

## *3.4 Testing for relationships: Correlations*

Correlations are conducted to determine presence, strength and direction of linear relationships between variables measured on continuous or deemed continuous scales. If a relationship exists between two variables, the Pearson correlation co-efficient (r) is statistically significant at below either the 0.01 or 0.05 level. The Pearson correlation co-efficient has a value between +1 and -1. A value of 0 indicates no relationship while a value of +1 or -1 indicates the value of one variable can be determined exactly by knowing the value of the other variable (linear relationship). The sign of the correlation co-efficient indicates the direction of the relationship. With a positive correlation, as the value of one variable increases, so too does the value of the other variable. With a negative correlation, as one variable increases, the other decreases. There are a range of different ways to interpret correlations but the most commonly used is that suggested by Cohen (1928) with an r value of .10 − .29 considered small or weak; .30 − .49 medium or moderate; and .50 to 1.0 large or strong.[13] Correlations do not distinguish between IVs and DVs and were conducted at the 95% confidence level.

Correlations were conducted to answer questions such as: Is there a relationship between trust in sources of health information and frequency of engaging in health-related behaviours?

[13] See Jacob Cohen, *Statistical power analysis for the behavioral sciences* (Lawrence Erlbaum Associates, 2e, 1988), 79-81.

## 3.5 Predicting group memberships: Multinomial logistic regression

Logistic regression is used to predict group membership by calculating the probability respondents will belong in one particular group as opposed to another group.[14] Multinomial logistic regression (MLR) is a type of logistic regression that predicts the probabilities of different possible outcomes in a categorical DV given a set of predictor variables (IVs). There are no constraints on the type of IV that can be used. The IV can be dichotomous (2 groups), categorical (more than two groups) or continuous (on a scale). MLR is used when the DV has two or more categories that cannot be ordered in a meaningful way, such as drug behavioural intention with its discrete increase, decrease, not change or consult doctor options.

One of the DV categories is selected as the reference group with probabilities determined relative to that group. In MLR, the term group refers to each individual answer option or category in the DV.MLR calculates the preference for each individual DV category compared to the reference group category in paired analyses. MLR is also fairly robust in predicting group membership for unequal group sizes.

MLR analysis determines significance (p value), interpreted as per other tests, and an odds ratio indicating how much the odds of being in one group (DV category) as opposed to the paired DV category increase or decrease for each predictor variable (IV). An odds ratio of 1 : 1 would indicate a 50/50 or equal chance, indicating the predictor variable does not have a significant impact on the DV category confirming MLR's default null hypothesis of no relationship between IV and DV. An odds ratio of 1 : 5.75 however would indicate a 475% chance of being in one group, with the predictor variable (IV) having substantial impact.

Odds ratios are determined from Exp(B) statistics. If the B statistic is positive, an Exp(B) of 1.725 would be interpreted as 72.5%. If the B statistic is negative, the odds ratio is calculated by dividing 1 by Exp(B) e.g. 1 divided by an Exp(B) of -.767 (or 1.304) would be interpreted as 30.4%.

Interpretation differs based on predictor variable (IV) type. For categorical variables, percentages reflect the increased likelihood of preference for one outcome versus another. For example, in the case of country, a 100% odds ratio indicates Australian respondents are twice as likely to prefer one outcome over another compared to US respondents.

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[14] See David Cox, 'The regression analysis of binary sequences (with discussion)' (1958) 20 *J Roy Stat Soc B*. 215-242.

For continuous variables, percentages reflect the increased likelihood of preference for one outcome versus another with each one-unit increase in the predictor variable (IV). For example, in the case of *emotional distress*, a 50% odds ratio would indicate a 50% increase in likelihood of preference for a particular outcome as *emotional distress* (IV) increases from 1 to 2, a 150% increase from 1 to 3, a 200% increase from 1 to 4 and a 250% increase from 1 to 5.

MLR analysis was conducted for the classification test (drug sensitivity) to answer questions such as: Is it possible to predict a respondent's behavioural intention relative to their medication regime based on the level of *emotional distress* experienced? (IV = *emotional distress*; DV = behavioural intention)

# APPENDIX FOUR: EXPLORATORY AND CONFIRMATORY FACTOR ANALYSIS

This analysis was conducted for the same ten psychological outcome variables used in the diabetes, cancer and drug sensitivity experiments, the fourteen behavioural intention variables used in each of the diabetes and cancer experiments, and the thirteen health-related attitude variables (health consciousness, health fatalism and causation). As only one behavioural intention variable was used for drug sensitivity, exploratory and confirmatory factor analyses were not appropriate.

Exploratory factor analysis suggested underlying factors did exist, warranting further exploration through Confirmatory factor analysis. CFA was conducted using MPLUS Version 7 with the Satorra-Bentler estimation method used in all models due to significant multivariate skewness.[15]

## *4.1 Confirmatory factor analysis: Psychological outcomes – Type 2 Diabetes*

The first model tested whether one factor existed across the full sample (n = 2000 representing the 1000 respondents each from Australia and the United States). Results revealed this model was an acceptable fit with the data: $\chi 2$ (35) = 334.33, $p < 0.001$, scaling correction factor = 1.8774, Comparative Fit Index (CFI) = 0.97, Tucker-Lewis Fit Index (TLI) = 0.95, Root Mean Square Error of Approximation (RMSEA) = 0.07, Standardized Root Mean Square Residual (SRMR) = 0.03.

The scaling correction factor was used to compare the $\chi^2$ across models as required when the Satorra-Bentler estimation procedure is used. The factor represents the extent to which multivariate nonnormality distorts the chi-square ($\chi^2$) derived from using standard or default maximum likelihood estimation.[16] CFI, TLI, RMSEA and SRMR are tests conducted to determine fit between data and model.[17] Acceptable model fit was determined by a CFI and TLI ≥ 0.95 and RMSEA and SRMR values < 0.05.

However, given that the RMSEA was arguably over the acceptable cut-off point of 0.05 (with 0% probability that the value was under 0.05), the modification indices (MIs) were inspected to assess possible improvements to the model. MIs provide guidance as to how a poor fitting model might be modified. Values represent an estimate of the expected reduction in the $\chi^2$ statistic,

[15] Linda Muthén and Bengt Muthén, *Mplus User's Guide* 6e (Muthén & Muthén, 1998-2010).
[16] See Fred Bryant and Albert Satorra, 'Principles and Practice of Scaled Difference Chi-square Testing' (2012) 19(3) *Structured Equation Modelling: A Multidisciplinary Journal* 372-398.
[17] Linda Muthén and Bengt Muthén, *Mplus User's Guide* 6e (Muthén & Muthén, 1998-2010).

where a lower $\chi^2$ represents better fit between the specified model and the associations present within the actual or observed data.

Large MIs were found for the covariance between concern and interest (MI = 96.09) and between concern and worry (MI = 97.64). The addition of a covariation between worry and interest was also suggested to improve the fit (MI = 19.06). The suggested inter-relationships between these three variables were thought to possibly indicate the presence of an additional factor that might represent *engagement* with the test results rather than *emotional distress*. A two-factor model was tested with one factor labelled *emotional distress* and the other *engagement*.

This 2-factor model was a good fit with the data: $\chi 2$ (34) = 196.64, $p < 0.001$, scaling correction factor = 1.8412, CFI = 0.98, TLI = 0.98, RMSEA = 0.05, SRMR = 0.03. The correlation between the two factors was very high ($r = 0.94$, $p < 0.001$) indicating that high *emotional distress* was strongly associated with high *engagement*. However, a scaled chi-square difference test revealed that the 2-factor model was a significantly better fit with the data than the 1-factor model: $\Delta\chi 2$ (1) = 85.46, $p < 0.001$. The factor loadings (Table 1) revealed that all items significantly and highly represented their corresponding factor, although the items relieved and interested were somewhat lower (although still highly significant).

**Table 4.1. Standardised Regression weights for 2-factor model**

| Factor | Standardised estimate[1] | Standard error | Factor score coefficient | Weight |
|---|---|---|---|---|
| *Emotional distress* | | | | |
| Anxious | 0.13 | 0.01 | 0.13 | 0.17 |
| Upset | 0.13 | 0.01 | 0.13 | 0.17 |
| Guilty | 0.04 | 0.02 | 0.04 | 0.05 |
| Relieved[2] | 0.01 | 0.03 | 0.01 | 0.01 |
| Scared | 0.90 | 0.01 | 0.14 | 0.18 |
| Nervous | 0.92 | 0.01 | 0.17 | 0.22 |
| Stressed | 0.90 | 0.01 | 0.14 | 0.18 |
| *Engagement* | | | | |
| Concerned | 0.84 | 0.01 | 0.14 | 0.24 |
| Interested | 0.44 | 0.02 | 0.03 | 0.05 |
| Worried | 0.95 | 0.01 | 0.42 | 0.71 |

[1] All estimates were significant at $p < 0.001$. [2] Relieved was reverse scored prior to calculating the weighted total score.

*Comparison of factor structures across countries*

To check the factor structure was equivalent across the AU and US samples, two 2-factor CFAs were computed. The first model consisted of a fully constrained 2-factor model identical to that tested above. In the fully constrained model, all factor loadings, correlations and error variances were forced to be equal across the AU and US samples. The results of the fully constrained model (Model 1) were not an acceptable fit with the data: $\chi 2$ (89) = 665.25, $p < 0.001$, CFI = 0.97, TLI = 0.97, RMSEA = 0.08, SRMR = 0.12.

This suggested the factor loadings were not statistically equal across countries so Wald tests were conducted on a fully unconstrained model. Wald tests determine whether a parameter (e.g. a factor loading regression weight) is significantly different across groups. Standard error calculations are necessary for conducting Wald tests.

In the unconstrained model, factor loadings and the correlation between factors were allowed to vary across country resulting in the data presented in Tables 2 and 3. The fully unconstrained model was a good fit with the data: $\chi 2$ (68) = 437.807, $p < 0.001$, CFI = 0.98, TLI = 0.97, RMSEA = 0.07, SRMR = 0.03.

**Table 4.2. Standardised Regression weights for 2-factor Type 2 Diabetes model (AU)**

| Factor – Type 2 Diabetes | Standardised estimate[1] | Standard error | Factor score coefficient | Weight |
|---|---|---|---|---|
| *Emotional distress* | | | | |
| Anxious | 0.90 | 0.01 | 0.16 | 0.11 |
| Upset | 0.88 | 0.01 | 0.13 | 0.13 |
| Guilty | 0.66 | 0.02 | 0.04 | 0.04 |
| Relieved[2] | -0.40 | 0.03 | 0.02 | 0.01 |
| Scared | 0.89 | 0.01 | 0.15 | 0.13 |
| Nervous | 0.91 | 0.01 | 0.18 | 0.16 |
| Stressed | 0.90 | 0.01 | 0.16 | 0.12 |
| *Engagement* | | | | |
| Concerned | 0.85 | 0.01 | 0.16 | 0.24 |
| Interested | 0.35 | 0.03 | 0.02 | 0.03 |
| Worried | 0.95 | 0.01 | 0.48 | 0.73 |
| Correlation | | | | |
| | 0.93 | 0.01 | | |

[1] All estimates were significant at $p < 0.001$. [2] Relieved was reverse scored prior to calculating the weighted total score.

**Table 4.3. Standardised Regression weights for 2-factor Type 2 Diabetes model (US)**

| Factor – Type 2 Diabetes | Standardised estimate[1] | Standard error | Factor score coefficient | Weight |
|---|---|---|---|---|
| *Emotional distress* | | | | |
| Anxious | 0.89** | 0.01 | 0.19 | 0.16 |
| Upset | 0.90*** | -.01 | 0.15 | 0.19 |
| Guilty | 0.70** | 0.02 | 0.05 | 0.05 |
| Relieved[2] | -0.26* | 0.03 | 0.02 | 0.01 |
| Scared | 0.90*** | 0.01 | 0.22 | 0.23 |
| Nervous | 0.92*** | 0.01 | 0.22 | 0.23 |
| Stressed | 0.90*** | 0.01 | 0.19 | 0.18 |
| *Engagement* | | | | |
| Concerned | 0.84* | 0.01 | 0.24 | 0.25 |
| Interested | 0.50*** | 0.03 | 0.03 | 0.07 |
| Worried | 0.94*** | 0.01 | 0.73 | 0.68 |
| Correlation | | | | |
| | 0.94 | 0.01 | | |

[1] All estimates were significant at $p < 0.001$. Wald tests for differences between countries: * $p < 0.05$; ** $p < 0.01$, *** $p < 0.001$. [2] Relieved was reverse scored prior to calculating the weighted total score.

Although all factor loadings were significantly different across countries, all differences were small. However, to account for the differential ability of each indicator to assess its underlying factor, weighted proportions for each variable were calculated from the factor score coefficients separately for each country (Tables 2 and 3). Total *emotional distress* scores were calculated for each of the seven indicators by multiplying the actual item score with the weight and then computing a total summed score. Similarly, a weighted total *engagement* score was calculated across the three engagement indicators.

## 4.2 Confirmatory factor analysis: Psychological outcomes – Colorectal Cancer

Again, results revealed a 1-factor model was not an acceptable fit with the data: $\chi 2$ (35) = 435.857, $p < 0.001$, scaling correction factor = 1.7469, CFI = 0.96, TLI = 0.95, RMSEA = 0.08, SRMR = 0.04. The 2-factor model was a significantly better fit ($\Delta\chi 2$ (1) = 57.00, $p < 0.001$) than the 1-factor model: $\chi 2$ (34) = 346.888, $p < 0.001$, scaling correction factor = 1.7118, CFI = 0.97, TLI = 0.96, RMSEA = 0.07, SRMR = 0.04. As with the Type 2 Diabetes analysis, the correlation between the two factors was very high ($r = 0.96$, $p < 0.001$) indicating that high *emotional distress* was strongly associated with high *engagement*.

*Comparison of factor structures across countries*

To check the factor structure was equivalent across the AU and US samples, two 2-factor CFAs were computed. The first model consisted of a fully constrained 2-factor model but this model (Model 1) were not an acceptable fit with the data: $\chi 2$ (89) = 800.795, $p < 0.001$, CFI = 0.96, TLI = 0.96, RMSEA = 0.09, SRMR = 0.14.

To determine whether the factor loadings were significantly different across countries, Wald tests were conducted on a fully unconstrained model. The results of this analysis along with the standardized factor loadings for the AU and US samples is presented in Tables 4 and 5. The fully unconstrained model was an acceptable fit with the data: $\chi 2$ (68) = 639.337, $p < 0.001$, CFI = 0.97, TLI = 0.96, RMSEA = 0.09, SRMR = 0.04.

**Table 4.4. Standardised Regression weights for 2-factor Colorectal Cancer model (AU)**

| **Factor – Colorectal Cancer** | **Standardised estimate[1]** | **Standard error** | **Factor score coefficient** | **Weight** |
|---|---|---|---|---|
| *Emotional distress* | | | | |
| Anxious | 0.92 | 0.01 | 0.16 | 0.21 |
| Upset | 0.90 | 0.01 | 0.13 | 0.16 |
| Guilty | 0.55 | 0.02 | 0.02 | 0.03 |
| Relieved[2] | -0.33 | 0.03 | 0.01 | 0.01 |
| Scared | 0.91 | 0.01 | 0.15 | 0.19 |
| Nervous | 0.92 | 0.01 | 0.15 | 0.20 |
| Stressed | 0.92 | 0.01 | 0.16 | 0.20 |
| *Engagement* | | | | |
| Concerned | 0.87 | 0.01 | 0.16 | 0.29 |
| Interested | 0.44 | 0.03 | 0.03 | 0.05 |
| Worried | 0.94 | 0.01 | 0.36 | 0.66 |
| Correlation | | | | |
| | 0.96 | 0.01 | | |

[1] All estimates were significant at $p < 0.001$. [2] Relieved was reverse scored prior to calculating the weighted total score.

**Table 4.5. Standardised Regression weights for 2-factor Colorectal Cancer model (US)**

| Factor – Colorectal Cancer | Standardised estimate[1] | Standard error | Factor score coefficient | Weight |
|---|---|---|---|---|
| *Emotional distress* | | | | |
| Anxious | 0.92*** | 0.01 | 0.11 | 0.17 |
| Upset | 0.92*** | 0.01 | 0.11 | 0.16 |
| Guilty | 0.65*** | 0.02 | 0.02 | 0.03 |
| Relieved[2] | -0.23 | 0.03 | 0.01 | 0.01 |
| Scared | 0.93*** | 0.01 | 0.12 | 0.18 |
| Nervous | 0.95*** | 0.00 | 0.17 | 0.25 |
| Stressed | 0.93*** | 0.01 | 0.13 | 0.19 |
| *Engagement* | | | | |
| Concerned | 0.88 | 0.01 | 0.13 | 0.28 |
| Interested | 0.53 | 0.02 | 0.03 | 0.06 |
| Worried | 0.95 | 0.01 | 0.30 | 0.65 |
| Correlation | | | | |
| | 0.96 | 0.01 | | |

[1] All estimates were significant at $p < 0.001$. Wald tests for differences between countries: * $p < 0.05$; ** $p < 0.01$, *** $p < 0.001$. [2] Relieved was reverse scored prior to calculating the weighted total score.

Although the factor loadings were significantly different across countries, all differences were small. However, to account for the differential ability of each indicator to assess its underlying factor, weighted proportions for each variable were calculated from the factor score coefficients separately for each country (Tables 4 and 5). Total *emotional distress* scores were calculated for each of the seven indicators by multiplying the actual item score with the weight and then computing a total summed score. Similarly, a weighted total *engagement* score was calculated across the three indicators.

## 4.3 Confirmatory factor analysis: Psychological outcomes – Drug sensitivity

Results revealed a 1-factor model was not an acceptable fit with the data: $\chi 2\ (35) = 564.953$, $p < 0.001$, scaling correction factor = 1.8758, CFI = 0.94, TLI = 0.92, RMSEA = 0.09, SRMR = 0.05. The 2-factor model was a significantly better fit ($\Delta\chi 2\ (1) = 73.36$, $p < 0.001$) than the 1-factor model: $\chi 2\ (34) = 466.521$, $p < 0.001$, scaling correction factor = 1.8526, CFI = 0.95, TLI = 0.93, RMSEA = 0.08, SRMR = 0.05.

The 2-factor model however was still not a good fit overall with the data. The regression weight (standardized) for the item Relieved suggested it was not a good indicator of Emotional distress (estimate = .12, $p < 0.001$) so it was removed from the model. The MI's for the item Worry (MI = 122.39) demonstrated poor discriminant validity as an indicator of Engagement and it was removed from the model. Relief and worry may not be an individual's expected reaction to receiving information about their drug metabolism rates as it would in relation to news of their relative risk of developing a disease such as Colorectal Cancer. Removing relieved and worry from the 2-factor model resulted in a good fit with the data: $\chi 2$ (19) = 175.572, $p < 0.001$, scaling correction factor = 1.9152, CFI = 0.98, TLI = 0.96, RMSEA = 0.06, SRMR = 0.03.

### *Comparison of factor structures across countries*

To check the factor structure was equivalent across the AU and US samples, two 2-factor CFAs were computed. The first model consisted of a fully constrained 2-factor model with all factor loadings, correlations and error variances forced to be equal across the AU and US samples. The results of the fully constrained model (Model 1) indicated that the model was not an acceptable fit with the data: $\chi 2$ (61) = 349.213, $p < 0.001$, scaling correction factor = 1.7719, CFI = 0.96, TLI = 0.96, RMSEA = 0.07, SRMR = 0.14.

To determine which factor loadings were significantly different across countries, Wald tests were conducted for each factor loading across country on a fully unconstrained model. The results of this analysis along with the standardized factor loadings for the AU and US samples is presented in Tables 6 and 7. The fully unconstrained model was an acceptable fit with the data: $\chi 2$ (44) = 221.211, $p < 0.001$, CFI = 0.97, TLI = 0.97, RMSEA = 0.06, SRMR = 0.03. The contribution to $\chi 2$ from each country suggested that the 2-factor model was a better fit for the US (97.25) than the AU sample (123.96).

With the exception of concerned, all of the factor loadings were again significantly different across the two countries. As such, different weights were used for AU and US respondents to compute *emotional distress* and *engagement* scores (Tables 6 and 7).

**Table 4.6. Standardised Regression weights for 2-factor Drug sensitivity model (AU)**

| Factor – Drug sensitivity | Standardised estimate[1] | Standard error | Factor score coefficient | Weight |
|---|---|---|---|---|
| *Emotional distress* | | | | |
| Anxious | 0.88 | 0.02 | 0.16 | 0.15 |
| Upset | 0.89 | 0.01 | 0.19 | 0.19 |
| Guilty | 0.69 | 0.03 | 0.05 | 0.05 |
| Scared | 0.91 | 0.01 | 0.22 | 0.21 |
| Nervous | 0.90 | 0.01 | 0.20 | 0.19 |
| Stressed | 0.91 | 0.01 | 0.22 | 0.21 |
| *Engagement* | | | | |
| Concerned | 1.21 | 0.08 | 0.37 | 0.72 |
| Interested | 0.36 | 0.05 | 0.14 | 0.28 |
| Correlation | | | | |
| | 0.593 | 0.048 | | |

[1] All estimates were significant at $p < 0.001$.

**Table 4.7. Standardised Regression weights for 2-factor Drug sensitivity model (US)**

| Factor – Drug sensitivity | Standardised estimate[1] | Standard error | Factor score coefficient | Weight |
|---|---|---|---|---|
| *Emotional distress* | | | | |
| Anxious | 0.90*** | 0.01 | 0.15 | 0.18 |
| Upset | 0.89*** | 0.01 | 0.15 | 0.17 |
| Guilty | 0.67*** | 0.02 | 0.04 | 0.05 |
| Scared | 0.91*** | 0.01 | 0.17 | 0.20 |
| Nervous | 0.92*** | 0.01 | 0.19 | 0.22 |
| Stressed | 0.90*** | 0.01 | 0.16 | 0.18 |
| *Engagement* | | | | |
| Concerned | 0.995 | 0.023 | 0.383 | 0.6951 |
| Interested | 0.551*** | 0.032 | 0.168 | 0.3049 |
| Correlation | | | | |
| | .741* | .028 | | |

[1] All estimates were significant at $p < 0.001$. Wald tests for differences between countries: * $p < 0.05$; ** $p < 0.01$, *** $p < 0.001$.

Although the factor loadings were significantly different across countries, all differences were small. However, to account for the differential ability of each indicator to assess its underlying factor, weighted proportions for each variable were calculated from the factor score coefficients separately for each country (Tables 6 and 7). Total *emotional distress* scores were calculated for each of the six indicators by multiplying the actual item score with the weight and then computing a total summed score. Similarly, a weighted total *engagement* score was calculated across the two engagement indicators.

## 4.4 Confirmatory factor analysis: Behavioural intention – Type 2 Diabetes

Initial exploratory factor analysis was conducted on the fourteen behavioural intention variables for the full sample (n = 2000) as the fourteen questions were quite distinct and it was doubtful that they would all load into one factor. This was confirmed in the EFA, which revealed five factors best fit the data. However, the item Not share with friends cross-loaded on three factors, demonstrating poor discriminant validity and inadequate construct validity (< 0.43 for each) and was removed. The four factors were labelled *Engage with healthcare professionals*, *Share and seek information*, *Engage in proactive health behaviours* and *Take no action*. As the item *Share with family* only loaded with Not share with friends, it was treated as a single indicator.

The resulting 4-factor model plus Share with family was tested for the full sample but was not an acceptable fit: $\chi 2$ (56) = 1075.16, $p < 0.001$, scaling correction factor = 1.3478, CFI = 0.86, TLI = 0.80, RMSEA = 0.10, SRMR = 0.08. Modification indices suggested the item Counsellor was also an indicator the factor Share and seek information (MI = 298.410) – EFA results suggested it as an indicator of the Engage with healthcare professionals factor. Since counselling may be provided online as well as traditionally (i.e. face to face) it was decided to include a direct effect between both factors and the Counsellor item. Modification indices suggested the item Online – not Dr was also indicator of the Engage with healthcare professionals factor was high (MI = 145.406) – EFA results indicated it as an indicator of the Share and seek information factor. As seeking help online rather than via healthcare professionals represents a preference, it was decided to include a direct effect between both factors and the Online – not Dr item.

The 5-factor modified model (4 factors plus Share with family) was a reasonable fit with the data, $\chi 2$ (54) = 594.128, scaling correction factor = 1.3392, $p < 0.001$, CFI = 0.93, TLI = 0.89, RMSEA = 0.07, SRMR = 0.05.

### *Comparison of factor structures across countries*

To check the factor structure was equivalent across the AU and US samples, a series of multi-sample CFAs were computed. A fully constrained model[18] was not an acceptable fit with the data, $\chi 2$ (143) = 846.65, $p < 0.001$, scaling correction factor = 1.2992, CFI = 0.90, TLI = 0.89, RMSEA = 0.07, SRMR = 0.11. A fully unconstrained model[19] was a significantly better fit with the data than

[18] Factor loadings, correlations and error variances were forced to be equal across individual AU and US samples.
[19] Factor loadings and the correlation between factors were allowed to vary across country.

the constrained model, $\Delta\chi 2$ (27) = 171.44, $p < 0.001$, $\chi 2$ (116) = 675.37, scaling correction factor = 1.3025, $p < 0.001$, CFI = 0.92, TLI = 0.90, RMSEA = 0.07, SRMR = 0.06.

To determine whether factor loadings were significantly different across countries, Wald tests were conducted for each factor loading across country on the fully unconstrained model (Tables 8 and 9). Given the numerous differences in the regression weights across countries, weighted proportions for each variable were calculated from the factor score coefficients separately for each country for Engage with healthcare professionals, Share and seek information, Engage in proactive health behaviours and Take no action. Share with family was treated as a factor in its own right by using the score from the original item.

**Table 4.8. Standardised Regression weights for 4 factors for Type 2 Diabetes (AU)**

| Factor – Type 2 Diabetes | Standardised estimate[1] | Standard error | Factor score coefficient | Weight |
|---|---|---|---|---|
| *Engage with healthcare professionals* | | | | |
| Confirm – doctor | 0.82 | 0.02 | 0.244 | 0.28 |
| Special appt | 0.87 | 0.02 | 0.337 | 0.38 |
| Doctor – interpret | 0.85 | 0.02 | 0.30 | 0.34 |
| Counsellor | 0.30 | 0.03 | 0.049 | 0.06 |
| Online – not Dr | -0.33 | 0.04 | -0.05 | -0.06 |
| *Share and seek information* | | | | |
| Online info | 0.56 | 0.04 | 0.149 | 0.14 |
| Share online | 0.58 | 0.03 | 0.152 | 0.15 |
| Online – others | 0.80 | 0.02 | 0.382 | 0.37 |
| Online – not Dr | 0.67 | 0.03 | 0.21 | 0.20 |
| Counsellor | 0.49 | 0.03 | 0.146 | 0.14 |
| *Engage in proactive health behaviours* | | | | |
| Monitor health | 0.80 | 0.03 | 0.445 | 0.57 |
| Change diet | 0.77 | 0.02 | 0.334 | 0.42 |
| *Take no action* | | | | |
| No decisions | 0.62 | 0.04 | 0.323 | 0.44 |
| Exercise same | 0.70 | 0.05 | 0.417 | 0.56 |

[1] All estimates were significant at $p < 0.001$. Share with family was treated as a single indicator so is not included in this table.

**Table 4.9. Standardised Regression weights for 4 factors for Type 2 Diabetes (US)**

| Factor – Type 2 Diabetes | Standardised estimate[1] | Standard error | Factor score coefficient | Weight |
|---|---|---|---|---|
| *Engage with healthcare professionals* | | | | |
| Confirm – doctor | 0.83 | 0.02 | 0.223 | 0.30 |
| Special appt | 0.896*** | 0.01 | 0.34 | 0.45 |
| Doctor – interpret | 0.794 | 0.02 | 0.173 | 0.23 |
| Counsellor | 0.297 | 0.04 | 0.059 | 0.08 |
| Online – not Dr | -0.447* | 0.06 | -0.046 | -0.06 |
| *Share and seek information* | | | | |
| Online info | 0.68** | 0.026 | 0.158 | 0.21 |
| Share online | 0.62** | 0.028 | 0.102 | 0.13 |
| Online – others | 0.73 | 0.022 | 0.175 | 0.23 |
| Online – not Dr | 0.94*** | 0.054 | 0.222 | 0.29 |
| Counsellor | 0.48 | 0.036 | 0.11 | 0.14 |
| *Engage in proactive health behaviours* | | | | |
| Monitor health | 0.80** | 0.02 | 0.297 | 0.48 |
| Change diet | 0.83*** | 0.019 | 0.328 | 0.52 |
| *Take no action* | | | | |
| No decisions | 0.55 | 0.045 | 0.211 | 0.32 |
| Exercise same | 0.78** | 0.052 | 0.456 | 0.68 |

[1] All estimates were significant at $p < 0.001$. Wald tests for differences between countries: * $p < 0.05$; ** $p < 0.01$, *** $p < 0.001$. Share with family was treated as a single indicator so is not included in this table.

## 4.5 Confirmatory factor analysis: Behavioural intention – Colorectal Cancer

The five-factor modified model tested for Type 2 Diabetes was reproduced for the full sample using Colorectal Cancer data. The results revealed the model was an acceptable fit: $\chi 2$ (54) = 572.739, $p < 0.001$, scaling correction factor = 1.3303, CFI = 0.94, TLI = 0.92, RMSEA = 0.07, SRMR = 0.04. Share with family was also confirmed as a single indictor.

### *Comparison of factor structures across countries*

To check that the factor structure was equivalent across the AU and US samples, two 4-factor CFAs were computed. Model 1 consisted of a fully constrained model using the four factors and indicated a borderline fit with the data: $\chi 2$ (143) = 876.509, $p < 0.001$, CFI = 0.92, TLI = 0.91, RMSEA = 0.07, SRMR = 0.10. While this suggested that the factor structure was reasonably stable across countries, given the differences found for Type 2 Diabetes, it was decided to test for significant differences in the factor loadings.

The unconstrained model was a significantly better fit suggesting some differences in the parameters across countries: $\Delta\chi 2$ (26) = 72.85, $p < 0.001$, $\chi 2$ (116) = 773.25, scaling correction factor = 1.3008, $p < 0.001$, CFI = 0.91, TLI = 0.88, RMSEA = 0.08, SRMR = 0.07. Wald tests confirmed a number of significant differences in the estimates across countries (Tables 10 and 11). As such, total scores were calculated using weights generated from the two countries separately.

**Table 4.10. Standardised Regression weights for 4 factors for Colorectal Cancer (AU)**

| **Factor – Colorectal Cancer** | **Standardised estimate[1]** | **Standard error** | **Factor score coefficient** | **Weight** |
|---|---|---|---|---|
| *Engage with healthcare professionals* | | | | |
| Confirm – doctor | 0.904 | 0.012 | 0.303 | 0.36 |
| Special appt | 0.908 | 0.012 | 0.304 | 0.36 |
| Doctor – interpret | 0.882 | 0.012 | 0.242 | 0.29 |
| Counsellor | 0.301 | 0.032 | 0.033 | 0.04 |
| Online – not Dr | -0.323 | 0.033 | -0.037 | -0.04 |
| *Share and seek information* | | | | |
| Online info | 0.713 | 0.024 | 0.213 | 0.22 |
| Share online | 0.543 | 0.032 | 0.03 | 0.12 |
| Online – others | 0.77 | 0.022 | 0.264 | 0.27 |
| Online – not Dr | 0.789 | 0.029 | 0.251 | 0.26 |
| Counsellor | 0.498 | 0.033 | 0.127 | 0.13 |
| *Engage in proactive health behaviours* | | | | |
| Monitor health | 0.83 | 0.02 | 0.373 | 0.52 |
| Change diet | 0.822 | 0.018 | 0.337 | 0.48 |
| *Take no action* | | | | |
| No decisions | 0.686 | 0.053 | 0.447 | 0.60 |
| Exercise same | 0.569 | 0.051 | 0.292 | 0.40 |

[1] All estimates were significant at $p < 0.001$. Share with family was treated as a single indicator so is not included in this table.

**Table 4.11. Standardised Regression weights for 4 factors for Colorectal Cancer (US)**

| Factor – Colorectal Cancer | Standardised estimate[1] | Standard error | Factor score coefficient | Weight |
|---|---|---|---|---|
| *Engage with healthcare professionals* | | | | |
| Confirm – doctor | 0.887* | 0.012 | 0.27 | 0.36 |
| Special appt | 0.856* | 0.016 | 0.194 | 0.25 |
| Doctor – interpret | 0.888** | 0.014 | 0.267 | 0.35 |
| Counsellor | 0.348 | 0.035 | 0.05 | 0.06 |
| Online – not Dr | -0.211 | 0.036 | -0.023 | -0.03 |
| *Share and seek information* | | | | |
| Online info | 0.749** | 0.02 | 0.149 | 0.20 |
| Share online | 0.687*** | 0.023 | 0.028 | 0.13 |
| Online – others | 0.858*** | 0.013 | 0.264 | 0.34 |
| Online – not Dr | 0.846** | 0.032 | 0.158 | 0.21 |
| Counsellor | 0.49 | 0.035 | 0.094 | 0.12 |
| *Engage in proactive health behaviours* | | | | |
| Monitor health | 0.824** | 0.02 | 0.293 | 0.56 |
| Change diet | 0.786* | 0.022 | 0.228 | 0.44 |
| *Take no action* | | | | |
| No decisions | 0.618 | 0.046 | 0.307 | 0.45 |
| Exercise same | 0.705** | 0.046 | 0.415 | 0.55 |

[1] All estimates were significant at $p < 0.001$. Wald tests for differences between countries: * $p < 0.05$; ** $p < 0.01$, *** $p < 0.001$. Share with family was treated as a single indicator so is not included in this table.

## 4.6 Confirmatory factor analysis: Health-related attitudes

Exploratory factor analysis of the thirteen health-related attitude variables across the full sample (n = 2000) and maximum likelihood estimation suggested a two-factor model, explaining 38.79% of the variance (Table 12). The first factor was labelled *health active* indicating active involvement with health with the second labelled *health passive* suggesting passive involvement.

A CFA of the two-factor model across the full sample approached an acceptable fit with the data but suggested improvements: $\chi 2$ (64) = 388.309, $p < 0.001$, scaling correction factor = 1.3444, CFI = 0.93, TLI = 0.92, RMSEA = 0.05, SRMR = 0.05. The largest MIs suggested Family history not important – Diabetes was uniquely (and negatively) correlated with Family history important – Cancer (MI = 47.38). If family history is interpreted as indicative of genetic predisposition, the pattern of loadings was also not intuitive. While Family history not important – Diabetes loaded onto the factor suggesting passive involvement (e.g. no control over health), Family history important – Cancer loaded onto the factor suggesting active involvement (e.g. control over

health). As such, both were removed, as these two health-related attitudes appear to measure a distinct construct. However, testing these two as a third factor did not produce a good fit with the data.

A two-factor model with the two health-related attitudes removed was a good fit with the data: $\chi 2$ (43) = 195.40, $p < 0.001$, scaling correction factor = 1.3322, CFI = 0.96, TLI = 0.95, RMSEA = 0.04, SRMR = 0.04. The standardised regression weights for this model are in Table 12.

**Table 4.12. Standardised Regression weights for 2-factor Health-related attitudes model**

| Factor[2] | Standardised estimate[1] | Standard error |
|---|---|---|
| *Health active* | | |
| Health depends on self | 0.709 | 0.02 |
| Responsible for own health | 0.723 | 0.023 |
| Lifestyle important − Diabetes | 0.661 | 0.023 |
| Alert to changes | 0.632 | 0.023 |
| Can control genetics | 0.376 | 0.025 |
| Can prevent − Diabetes | 0.373 | 0.029 |
| *Health passive* | | |
| Cannot prevent illness | 0.737 | 0.019 |
| Cannot control genetics | 0.766 | 0.017 |
| Lifestyle not important − Cancer | 0.692 | 0.02 |
| Worry only when sick | 0.501 | 0.023 |
| Cannot prevent − Cancer | 0.553 | 0.021 |

[1] All estimates were significant at $p < 0.001$. [2] Correlations between health active and health passive = 0.245, $p < 0.001$.

### *Comparison of factor structures across countries*

To check the factor structure was equivalent for the eleven health-related attitudes across the AU and US samples, two 2-factor CFAs were computed. The first model consisted of a fully constrained 2-factor model identical to that tested above. In the fully constrained model, all factor loadings, correlations and error variances were forced to be equal across the AU and US samples. The results of the fully constrained model (Model 1) were not an acceptable fit with the data: $\chi 2$ (118) = 475.412, $p < 0.001$, CFI = 0.90, TLI = 0.91, RMSEA = 0.06, SRMR = 0.13.

An unconstrained model where factor loadings, residuals and the correlation between factors were allowed to vary across country was not a good fit with the data: $\chi 2$ (104) = 504.85, $p < 0.001$, Scaling correction factor = 1.31, CFI = 0.89, TLI = 0.89, RMSEA = 0.06, SRMR = 0.09. Numerous MI's for Can control genetics suggested that this health-related attitude was not a good indicator of health active for the AU sample and cross loaded with health passive for the US

sample. Other MI's suggested this health-related attitude also shared unique variance with multiple other items in both countries. It was therefore decided to remove this item. The resulting unconstrained model on the remaining 10 items was an acceptable fit with the data, $\chi 2$ (83) = 275.80, $p < 0.001$, scaling correction factor = 1.3366, CFI = 0.94, TLI = 0.94, RMSEA = 0.05, SRMR = 0.06. To investigate significant differences across the factor loadings and correlation between factors Wald tests were conducted on the fully unconstrained model (Tables 13 and 14).

**Table 4.13. Standardised Regression weights for 2-factor model (AU)**

| Factor | Standardised estimate[1] | Standard error | Factor score coefficient | Weight |
|---|---|---|---|---|
| *Health active* | | | | |
| Health depends on self | 0.693 | 0.029 | 0.323 | 0.217 |
| Responsible for own health | 0.770 | 0.025 | 0.472 | 0.317 |
| Lifestyle important − Diabetes | 0.662 | 0.031 | 0.276 | 0.185 |
| Alert to changes | 0.660 | 0.028 | 0.292 | 0.196 |
| Can prevent − Diabetes | 0.426 | 0.037 | 0.125 | 0.084 |
| *Health passive* | | | | |
| Cannot prevent illness | 0.664 | 0.033 | 0.287 | 0.238 |
| Cannot control genetics | 0.704 | 0.028 | 0.359 | 0.297 |
| Lifestyle not important − Cancer | 0.646 | 0.034 | 0.266 | 0.220 |
| Worry only when sick | 0.446 | 0.036 | 0.126 | 0.104 |
| Cannot prevent − Cancer | 0.516 | 0.032 | 0.170 | 0.141 |

[1] All estimates were significant at $p < 0.001$.

**Table 4.14. Standardised Regression weights for 2-factor model (US)**

| Factor | Standardised estimate[1] | Standard error | Factor score coefficient | Weight |
|---|---|---|---|---|
| *Health active* | | | | |
| Health depends on self | 0.726* | 0.023 | 0.393 | 0.283 |
| Responsible for own health | 0.691 | 0.038 | 0.363 | 0.261 |
| Lifestyle important − Diabetes | 0.648 | 0.033 | 0.283 | 0.204 |
| Alert to changes | 0.621 | 0.036 | 0.260 | 0.187 |
| Can prevent − Diabetes | 0.332 | 0.043 | 0.091 | 0.065 |
| *Health passive* | | | | |
| Cannot prevent illness | 0.781*** | 0.022 | 0.275 | 0.278 |
| Cannot control genetics | 0.797*** | 0.020 | 0.305 | 0.308 |
| Lifestyle not important − Cancer | 0.716*** | 0.024 | 0.199 | 0.201 |
| Worry only when sick | 0.532** | 0.030 | 0.100 | 0.101 |
| Cannot prevent − Cancer | 0.549** | 0.020 | 0.111 | 0.112 |

[1] All estimates were significant at $p < 0.001$. * = Wald test significant at $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Although health active and all health passive factor loadings were significantly different across countries, all differences were small. However, to account for the differential ability of each indicator to assess its underlying factor, weighted proportions for each variable were calculated from the factor score coefficients separately for each country (Tables 13 and 14). Total health active scores were calculated for each of the five health-related attitudes by multiplying the actual item score with the weight and then computing a total summed score. Similarly, a weighted total health passive score was calculated across the five health-related attitudes.

# APPENDIX FIVE: MANOVA ANALYSIS FOR TYPE 2 DIABETES & COLORECTAL CANCER PSYCHOLOGICAL OUTCOMES

## *Do Psychological outcomes differ by interpretation of DTCGT disease predisposition test results?*

To determine whether actual severity (allocated personal risk) and perceived severity (interpretation of personal risk) influenced the level of *emotional distress* and *engagement* experienced relative to diabetes and cancer, individual 3 (AS(Low), AS(High), AS(Higher)) by 4 (PS(Lower), PS (Higher), PS(Same), PS(Not sure)) Multivariate Analysis of Variance (MANOVA) were conducted. As the confirmatory factor analysis indicated *emotional distress* and *engagement* were highly correlated, a MANOVA was appropriate to assess mean differences across the 12 groups (3 x 4) for each disease. To investigate whether there were any unique effects for *emotional distress* and *engagement*, separate 3 x 4 ANOVAs for each disease were also conducted. To determine whether the influence of actual severity or perceived severity on *emotional distress* and *engagement* varied across country for each disease, a 3 (AS) x 4 (PS) x 2 (AU, US) MANOVA and individual ANOVAs were conducted.

## *Do psychological outcomes differ by interpretation of Diabetes DTCGT test results?*

### *Actual severity and perceived severity: Multivariate and univariate effects*

MANOVA analysis revealed a range of multivariate and univariate effects for actual severity, perceived severity and country. Multivariate analysis identifies the effect of actual severity and perceived severity (individually and in combination) on the two psychological outcome factors of *emotional distress* and *engagement* combined. Univariate analysis identifies the effect of actual severity and perceived severity (individually and in combination) on *emotional distress* and *engagement* individually. Main effects refer to the effects identified in the multivariate analysis.

### *What are the effects of actual severity and perceived severity individually?*

Multivariate results of the 3 (AS) x 4 (PS) MANOVA revealed significant main effects for both actual severity (**$F(4, 3950) = 2.80$, $p < 0.05$, $\eta^2 = 0.003$**) and perceived severity **($F(6, 3950) = 25.391$, $p < 0.001$, $\eta^2 = 0.037$**) individually on the combination of *emotional distress* and *engagement*.

Univariate results revealed that both *emotional distress* (**$F(2, 1976) = 4.409$, $p < 0.05$, $\eta^2 = 0.004$**) and *engagement* (**$F(2, 1976) = 5.358$, $p < 0.05$, $\eta^2 = 0.005$**) were influenced by actual severity. Similarly, both *emotional distress* (**$F(3, 1976) = 35.680$, $p < 0.001$, $\eta^2 = 0.051$**) and *engagement* (**$F(3, 1976) = 50.041$, $p < 0.001$, $\eta^2 = 0.071$**) were influenced by perceived severity. Comparison of the effect sizes

($\eta^2$) suggest the effect of perceived severity on *emotional distress* was almost thirteen times as strong as actual severity, and for *engagement* perceived severity was over fourteen times as strong as actual severity.

### *What is the effect of actual severity combined with perceived severity?*

Multivariate results revealed the interaction between actual severity and perceived severity was significant (**F (12, 3950) = 8.183, p < 0.001, $\eta^2$ = 0.024**). Univariate results revealed that both *emotional distress* (**F (6, 1976) = 15.124, p < 0.001, $\eta^2$ = 0.044**) and *engagement* (**F (6, 1976) = 8.174, p < 0.001, $\eta^2$ = 0.024**) were influenced by the interaction of actual severity and perceived severity. Univariate results however clearly showed the effects of the actual and perceived severity on either *emotional distress* or *engagement* depended primarily on perceived severity.

## *Country: Multivariate and univariate effects*

Multivariate analysis identified the effect of country (AU & US combined) alone and in combination with actual severity and/or perceived severity on *emotional distress* and *engagement combined*. Univariate analysis identifies the effect of country on its own and in combination with actual severity and/or perceived severity on *emotional distress* and *engagement* individually.

Results of the 3 x 4 x 2 MANOVA suggested significant multivariate effects for country on its own (**F [2, 1975] = 287.970, p < 0.001, $\eta^2$ = .226**); country in combination with perceived severity (**F [6, 3950] = 4.393, p < 0.001, $\eta^2$ = .007**); and country in combination with actual severity and perceived severity (**F [12, 3950] = 1.878, p < 0.05, $\eta^2$ = .006**). No multivariate effects were found for country in combination with actual severity as expected due to random allocation (F [4, 3950] = 2.129, p > 0.05, $\eta^2$ = .002).

There were also significant univariate effects for country on its own on *emotional distress* (**F [1, 1976] = 168.706, p < 0.001, $\eta^2$ = .079**) but not *engagement* (F [1, 1976] = 0.602, p > 0.05, $\eta^2$ = .000); country in combination with actual severity for both *emotional distress* (**F [2, 1976] = 3.240, p < 0.05, $\eta^2$ = .003**) and *engagement* (**F [2, 1976] = 3.829, p < 0.05, $\eta^2$ = .004**); and country in combination with perceived severity on *emotional distress* (**F [3, 1976] = 6.546, p < 0.001, $\eta^2$ = .010**) but not *engagement* (F [3, 1976] = 1.573, p > 0.05, $\eta^2$ = .002). No univariate effects were found for country in combination with actual severity and perceived severity on either *emotional distress* (F [6, 1976] = 0.858, p > 0.05, $\eta^2$ = .003) or *engagement* (F [6, 1976] = 1.691, p > 0.05, $\eta^2$ = .005).

## *How do emotional distress and engagement differ by Actual severity?*

Both mean *emotional distress* and mean *engagement* were lowest for respondents allocated AS(Low) and highest for respondents allocated AS(Higher). Mean *emotional distress* and *engagement* clearly increase as AS allocation changes (low →high →higher), with the effect more pronounced for *engagement* where mean scores much higher than *emotional distress* means were observed. For example, note the difference in mean *emotional distress* and *engagement* experienced by those allocated AS(High) compared with those allocated AS(Higher).

### *Does this differ by country?*

The same pattern of *emotional distress* and *engagement* increasing with increasing actual severity levels and mean *engagement* higher than mean *emotional distress* was exhibited in both countries. US respondents however experienced higher mean *emotional distress* and *engagement* at all actual severity levels. This was especially pronounced for *emotional distress* with greater differences in mean scores observed.

## *How do emotional distress and engagement differ by Perceived severity?*

Mean *emotional distress* and *engagement* experienced were lowest for respondents who interpreted their risk as lower and highest for respondents who interpreted their risk as higher. Again, mean *engagement* was higher than mean *emotional distress* in all instances.

### *Does this differ by country?*

The same pattern of *emotional distress* and *engagement* being lowest for those who interpreted their risk as lower and highest for respondents who interpreted their risk as higher was observed in both countries. Mean *engagement* scores were also higher than mean *emotional distress* scores in both countries. US respondents however experienced higher mean *emotional distress* and *engagement* at all perceived severity levels.

## *How do emotional distress and engagement differ by Actual severity and Perceived severity?*

In all instances, mean *engagement* was higher than mean *emotional distress*. Respondents allocated AS(Low) who interpreted their risk as higher experienced higher mean *emotional distress* and *engagement* than others in their AS allocation who interpreted their risk as lower. They also experienced higher mean *emotional distress* and *engagement* than respondents allocated AS(High) who interpreted the risk as higher.

Interestingly, respondents allocated AS(Low) who interpreted their results as the same or were unsure experienced higher mean *emotional distress* and *engagement* than those who interpreted their risk as lower. Respondents allocated AS(High) who interpreted their results as the same or were unsure experienced lower mean *emotional distress* and *engagement* than those in their AS allocation interpreting their risk as lower. Those allocated AS(Higher) interpreting their risk as the same experienced the same mean *emotional distress* and higher mean *engagement* than those interpreting the risk as lower.

Respondents allocated AS(High) who interpreted their risk as lower experienced higher mean *emotional distress* than those in their AS allocation interpreting their risk as higher. Interestingly, respondents allocated AS(High) and AS(Higher) who interpreted their risk as lower experienced higher levels of both *emotional distress* and *engagement* than respondents allocated AS(Low) who interpreted the risk as lower.

### *Does this differ by country?*

AU respondents allocated AS(Low) who interpreted their risk as higher experienced higher mean *emotional distress* and e*ngagement*. These respondents not only experienced higher levels of *emotional distress* and *engagement* than others in AS(Low) who interpreted their as lower but also respondents allocated AS(High) who interpreted their risk as higher. Respondents interpreting their risk as the same or who were unsure experienced higher mean *emotional distress* and *engagement* than those interpreting their risk as lower.

Respondents allocated AS(High) who interpreted their risk as lower experienced higher mean *emotional distress* and *engagement* compared to those who interpreted the results as higher. Interestingly these respondents also experienced higher mean *emotional distress* and *engagement* than respondents allocated AS(Low) who interpreted their risk as lower.

US respondents exhibited similar patterns. Those allocated AS(Low) who interpreted their risk as higher experienced higher *emotional distress* than those who interpreted their risk as lower and also higher than those allocated AS(High) and AS(Higher) who interpreted their risk as higher. They also experienced higher *engagement* not just compared to their counterparts who interpreted their risk as lower but also those allocated AS(High) who interpreted their risk as higher.

Again, respondents allocated into AS(High) and AS(Higher) who interpreted their risk as lower experienced higher mean *emotional distress* and *engagement* than respondents allocated into AS(Low) who interpreted their risk as lower.

## *Do psychological outcomes differ by interpretation of Cancer DTCGT test results?*

### *Actual severity and perceived severity: Multivariate and univariate effects*

MANOVA analysis revealed a range of multivariate and univariate effects for actual severity, perceived severity and country.

### *What are the effects of actual severity and perceived severity individually?*

Multivariate results of the 3 (AS) x 4 (PS) MANOVA revealed significant main effects for both actual severity (**F [4, 3950] = 6.690, p < 0.001, $\eta^2$ = .007**) and perceived severity (**F [6, 3950] = 32.702, p < 0.001, $\eta^2$ = .047**). Univariate results revealed that both *emotional distress* (**F [2, 1976] = 13.213, p < 0.001, $\eta^2$ = .013**) and *engagement* (**F [2, 1976] = 10.566, p < 0.001, $\eta^2$ = .011**) were influenced by actual severity. Similarly, both *emotional distress* (**F [3, 1976] = 50.588, p < 0.001, $\eta^2$ = .071**) and *engagement* (**F [3, 1976] = 64.829, p < 0.001, $\eta^2$ = .090**) were influenced by perceived severity.

Comparison of the effect sizes ($\eta^2$) suggest the effect of perceived severity on *emotional distress* was more than five times as strong as actual severity, and for *engagement* perceived severity was more than eight times as strong as actual severity. Additionally, perceived severity effect sizes for cancer were higher than those for diabetes (0.071 compared to 0.051 for *emotional distress* and 0.090 compared to 0.071 for *engagement*), suggesting perceived severity plays a more significant role for cancer.

### *What is the effect of actual severity combined with perceived severity?*

The interaction between actual severity and perceived severity was also significant for both the multivariate (**F [12, 3950] = 8.978, p < 0.001, $\eta^2$ = .027**) and all univariate results. The effects of actual severity on *emotional distress* and *engagement* depended on how the test results were interpreted (perceived severity). Both univariate interactions were significant (*emotional distress*: **F [6, 1976] = 13.504, p < 0.001, $\eta^2$ = .039**; *engagement*: **F [6, 1976] = 7.895, p < 0.001, $\eta^2$ = .023**), suggesting the combined effects of actual severity and perceived severity was evident for both *emotional distress* and *engagement*.

Multivariate results revealed the interaction between actual severity and perceived severity was significant (**F [12, 3950] = 8.978, p < 0.001, $\eta^2$ = .027**). Univariate results revealed that both *emotional distress* (**F [6, 1976] = 13.504, p < 0.001, $\eta^2$ = .039**) and *engagement* (**F [6, 1976] = 7.895, p < 0.001, $\eta^2$ = .023**) were influenced by the interaction of actual severity and perceived severity. Univariate results again clearly showed the effects of actual and perceived severity on either *emotional distress* or *engagemen*t depended primarily on perceived severity.

## *Country: Multivariate and univariate effects*

Results of the 2 x 4 x 3 MANOVA suggested there were no significant multivariate effects for country on its own (F [2, 1975] = 1.947, p > 0.05, $\eta^2$ = .002) or country in combination with actual severity and perceived severity (F [12, 3950] = 0.871, p > 0.05, $\eta^2$ = .003) on combined *emotional distress* and *engagement*. Multivariate effects however were found for country in combination with actual severity (**F [4, 3950] = 3.237, p < 0.05, $\eta^2$ = .003**)[20] and country in combination with perceived severity (**F [6, 3950] = 2.353, p < 0.05, $\eta^2$ = .004**).

There were also significant univariate effects for country on its own on *emotional distress* (**F [1, 1976] = 3.896, p < 0.05, $\eta^2$ = .002**) but not *engagement* (F [1, 1976] = 3.013, p > 0.05, $\eta^2$ = .002) and country in combination with actual severity for *engagement* (**F [2, 1976] = 3.082, p < 0.05, $\eta^2$ = .003**) but not *emotional distress* (F [2, 1976] = 0.797, p > 0.05, $\eta^2$ = .001). No significant univariate effects however were found for country in combination with perceived severity for either *emotional distress* (F [3, 1976] = 1.075, p > 0.05, $\eta^2$ = .002) or *engagement* (F [3, 1976] = 1.783, p > 0.05, $\eta^2$ = .003) and country in combination with both actual severity and perceived severity for either *emotional distress* (F [6, 1976] = 0.137, p < 0.05, $\eta^2$ = .000) or *engagement* (F [6, 1976] = 0.802, p > 0.05, $\eta^2$ = .002).

## *How do emotional distress and engagement differ by Actual severity?*

Mean *emotional distress* and *engagement* were lowest for respondents allocated AS(Low) and highest for respondents allocated AS(Higher). Mean *emotional distress* and *engagement* clearly changes as Actual severity allocation changes, with the effect more pronounced for *engagement* where mean scores much higher than *emotional distress* means were observed.

### *Does this differ by country?*

The same pattern was found in AU and US with *emotional distress* and *engagement* increasing with increasing actual severity and mean *engagement* higher than mean Emotional distress. No consistent pattern as to which country's respondents experienced higher mean *emotional distress* and *engagement* was identified.

[20] Despite random allocation into Actual severity group.

## *How do emotional distress and engagement differ by Perceived severity?*

Mean *emotional distress* and *engagement* experienced were lowest for respondents who interpreted their risk as lower and highest for respondents who interpreted their risk as higher. Again, mean *engagement* was also higher than mean *emotional distress* in all instances.

### *Does this differ by country?*

The same pattern of *emotional distress* and *engagement* being lowest for those who interpreted their risk as lower and highest for respondents who interpreted their risk as higher was observed in both countries. Mean *engagement* scores were also higher than mean *emotional distress* scores in both countries. AU respondents however experienced higher mean *emotional distress* and *engagement* at all perceived severity levels. The exception was *emotional distress* for those who interpreted their risk as higher where US respondents experienced slightly higher mean *emotional distress*.

## *How do emotional distress and engagement differ by Actual severity and Perceived severity?*

Respondents allocated AS(Low) who interpreted their risk as higher experienced higher mean *emotional distress* and *engagement* compared to others in their As allocation. These respondents also experienced higher mean *emotional distress* than respondents allocated AS(Higher) who interpreted their risk as higher. Respondents allocated AS(Low) who interpreted their risk as the same or were not sure experienced higher mean *emotional distress* and *engagement* compared to those interpreting the risk as lower: a pattern not observed for AS(High) or AS(Higher).

### *Does this differ by country?*

AU respondents allocated AS(Low) who interpreted their risk as higher experienced not only higher mean *emotional distress* compared with other respondents in their AS allocation but the highest mean *emotional distress* of all respondents. They also experienced higher mean e*ngagement* than those allocated AS(High) who interpreted their risk as higher.

Respondents allocated AS(Low) who interpreted their risk as the same or were unsure experienced higher mean *emotional distress* and *engagement* compared with those who interpreted their risk as lower. Respondents allocated AS(High) and AS(Higher) however who interpreted their results as the same actually experienced lower mean *emotional distress* and *engagement* than those who interpreted their risk as lower.

US respondents exhibited the same patterns as their AU counterparts. Those allocated AS(Low) who interpreted their results as higher experienced higher mean *emotional distress* and *engagement* than others in AS(Low). Those interpreting their results as the same or were unsure experienced higher mean *emotional distress* and *engagement* than those interpreting their risk as lower. Again, respondents allocated AS(High) and AS(Higher) who interpreted their results as the same experienced lower mean *emotional distress* and *engagement* than those who interpreted their risk as lower.

## *How do the two diseases compare?*

### *Do emotional distress and engagement differ by Actual severity?*

Respondents experienced much higher mean *emotional distress* for cancer and slightly higher mean *engagement* for diabetes.

Overall, the highest mean *emotional distress* was experienced by respondents allocated AS(Higher) for cancer. The highest mean *engagement* was experienced by respondents allocated AS(Higher) for diabetes.

### *Do emotional distress and engagement differ by Perceived severity?*

Respondents exhibited higher mean *emotional distress* for cancer in all instances. The results for *engagement* were not as clear-cut. Respondents exhibited mean *engagement* for diabetes if they interpreted the results as lower, same or not sure. However, respondents interpreting the results as higher exhibited higher levels of *engagement* for cancer.

Overall, respondents who interpreted their results as indicating a higher risk for cancer experienced the highest mean *emotional distress* and *engagement*.

## *Do emotional distress and engagement differ by Actual severity and Perceived severity?*

For all Actual severity groups and all perceived severity levels, mean *emotional distress* was higher for cancer. The pattern for mean *engagement* was not as clear-cut. In all instances, respondents allocated AS(Low) and AS(High) experienced higher mean *engagement* for diabetes at all perceived severity levels (with the exception of not sure for AS(High)). For those allocated AS(Higher), mean *engagement* was slightly higher for diabetes with the exception of those who interpreted the risk as lower for cancer.